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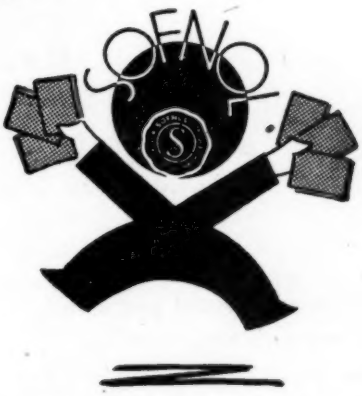

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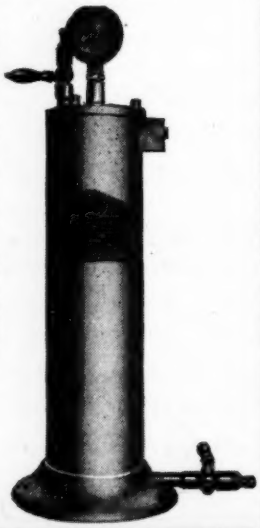

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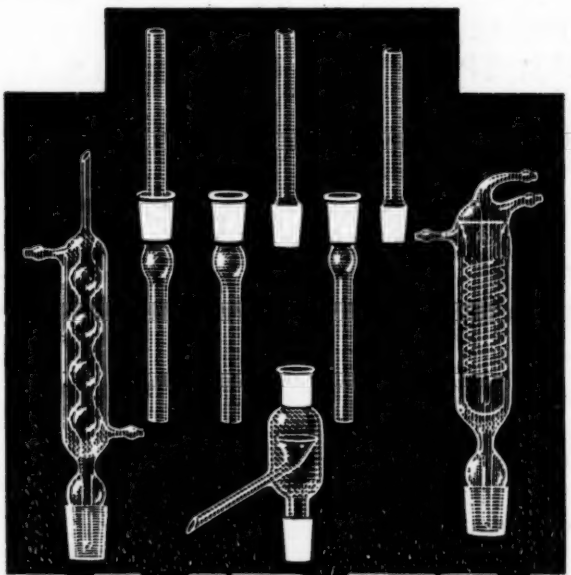

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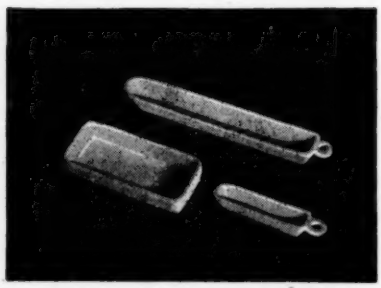

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ERRATA.

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Page.	Line.	
193	12*	*For* "$k_1 t = \frac{2{\cdot}303}{-\Delta} \log \frac{(x-a)}{a(x-\Delta)}$" *read* "$k_1 t = \frac{2{\cdot}303}{a-\Delta} \log \frac{\Delta(x-a)}{a(x-\Delta)}$."
518	19*	*For* "$\log_m \xi$" *read* "$\log \epsilon_m$."

* From bottom.

and as the phenylhydrazine evolves all its nitrogen in each reaction this fact does not invalidate Ellis's method. It does, however, interfere with any method, either gravimetric or volumetric, based on the amount of cuprous oxide precipitated. The following titrations show that at 93° the ratio of the two processes is materially influenced by the concentrations of the reactants employed.

It was thought probable that the particular process taking place would be largely determined by the oxidation potential, E, established in the complex cupric solution. For $Cu^{\cdot\cdot} \longrightarrow Cu^{\cdot} + F$

$$E_{Cu^{\cdot\cdot} \rightarrow Cu^{\cdot}} = \varepsilon_{Cu^{\cdot\cdot} \rightarrow Cu^{\cdot}} - (RT/F) \log_e [Cu^{\cdot}]/[Cu^{\cdot\cdot}]$$

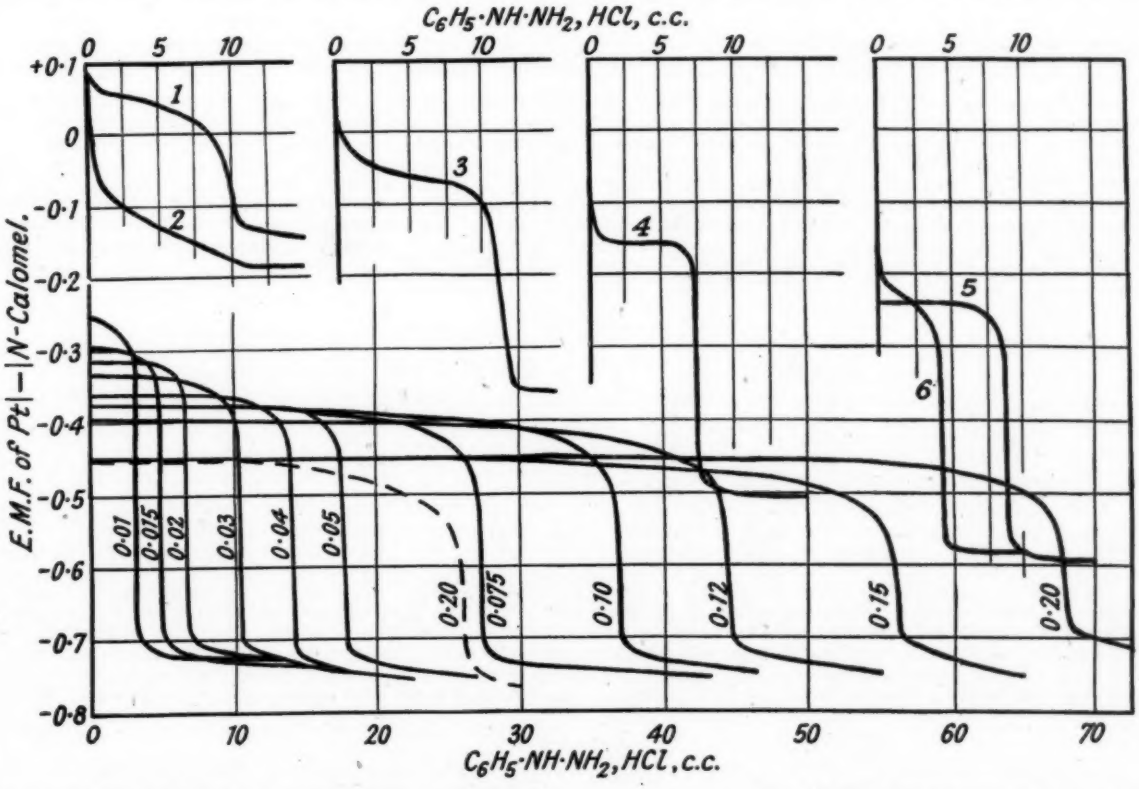
hence the actual oxidation potential, $E_{Cu^{\cdot\cdot} \rightarrow Cu^{\cdot}}$, will depend on the ratio $[Cu^{\cdot}]/[Cu^{\cdot\cdot}]$, and, as cuprous oxide is always precipitated, the $[Cu^{\cdot}]$ will be determined by $[OH']$, and consequently by the p_H. Similarly, the $[Cu^{\cdot\cdot}]$ will be governed by the concentration of the solution and the constitution of the complex cupric salt. For this reason the p_H of the complex alkaline cupric tartrate solution was varied by the introduction of alkaline buffers, *viz.*, borax and disodium hydrogen phosphate, and also the behaviour of other complex cupric solutions, which may be buffered in the acid and the neutral range, was investigated.

Experimental.

The titration cell used was

Pt	100 c.c. of Cu solution x c.c. of $C_6H_5 \cdot NH \cdot NH_2$,HCl	Satd. KCl	N-KCl	N-KCl Hg_2Cl_2	Hg

It was immersed in a water-bath, the temperature of which was regulated at 93° ± 1°. To prevent atmospheric oxidation, the titration cell was closed with a tightly fitting ebonite cap. Nitrogen was used to maintain an oxygen-free atmosphere above the solution and also to agitate the solution after each addition of titrant. To ensure that reproducible potentials were being indicated, two bright platinum electrodes were used and the *P.D.*'s between each electrode and the normal calomel electrode were measured.



Effect of Concentration of Fehling's Solution and Phenylhydrazine Hydrochloride Solution.—Some titrations were performed of phenylhydrazine hydrochloride with Fehling's solution as the titrant, but the potentials set up were not always steady, nor were the titration curves completely reproducible. Two difficulties were encountered: (i) the p_H varies over a wide range in the course of the titration, and (ii) the unattacked phenylhydrazine is appreciably volatile at 93°. The volatility was particularly evident in a series of titrations of phenylhydrazine in the presence of an excess of alkali added to stabilise the p_H. In consequence, the above procedure was reversed, the cupric solutions being titrated with phenylhydrazine hydrochloride. The presence of the combined hydrochloric acid in the latter did not introduce any great variations in the p_H of the solution undergoing titration as there was always present an excess of alkali or buffering agent.

The complex alkaline cupric tartrate solutions were prepared from copper sulphate, sodium tartrate, and sodium hydroxide in the molecular ratio 1 : 4·6 : 10 as used in Fehling's solution. Sodium tartrate was substituted for Rochelle

salt as previous work has shown that this change does not affect the oxidation. Table I gives details of the titrations of 100 c.c. of Fehling's solution, the initial concentrations of copper sulphate ranging from 0·01M to 0·2M. The phenylhydrazine hydrochloride was 0·1M, except in the cases of the 0·04M- and 0·2M-copper solutions, where it was 0·25M. These titrations are marked with an asterisk. For the titration marked †, twice the relative amount of alkali was present in the complex tartrate solution.

TABLE I.

$CuSO_4$, mols./l.	Titre, c.c.	$\frac{CuSO_4}{NH_2 \cdot NHPh}$	$NH_2 \cdot NHPh$, %, converted into C_6H_6.	$C_6H_5 \cdot OH$.	$CuSO_4$, mols./l.	Titre, c.c.	$\frac{CuSO_4}{NH_2 \cdot NHPh}$	$NH_2 \cdot NHPh$, %, converted into C_6H_6.	$C_6H_5 \cdot OH$.
0·010	3·29	3·03	48·5	51·5	0·050	17·66	2·83	58·5	41·5
†0·010	3·35	2·98	51	49	0·075	27·15	2·72	64	36
0·015	5·00	3·00	50	50	0·100	36·7	2·70	65	35
0·020	6·70	2·98	51	49	0·120	44·3	2·71	64·5	35·5
0·030	10·40	2·88	56	44	0·150	56·0	2·68	66	34
*0·040	14·05	2·85	57·5	42·5	0·200	67·8	2·95	52·5	47·5
0·040	5·55	2·87	56·5	43·5	*0·200	25·9	3·24	38	62

The titration curves are plotted in the lower part of the figure, the concentration of the copper sulphate being indicated on each curve. The curve represented as a broken line is a duplicate of the 0·2M-copper curve except that 0·25M-phenylhydrazine hydrochloride was used instead of 0·1M.

The curves show that, as the concentrations of the Fehling's solution are increased, the initial potentials become increasingly more negative, with respect to that of the normal calomel electrode, whereas the final potentials tend to acquire fairly constant values. This fact reduces the drop in potential which occurs at the inflexions when the cupric salt has been reduced entirely to cuprous oxide and the solutions have just become colourless. The curves show clearly that the optimum conditions for potentiometric titration occur when the copper sulphate concentration is very low, preferably 0·01—0·02M. Table I reveals that it is only with these concentrations that the phenylhydrazine is oxidised equally to benzene and phenol. (The data in cols. 4 and 5 were computed from those in col. 3 on the basis of the equations of the two simultaneous oxidations.) With copper sulphate concentrations from 0·03M to 0·15M, col. 3 shows that progressively less cupric salt is required to effect oxidation, with the result that the benzene produced increases to 66%.

Influence of p_H *on the Oxidising Action of Alkaline Cupric Tartrate Solutions.*—In order to ascertain whether p_H had any effect on the oxidising reactions occurring when 0·1M-phenylhydrazine hydrochloride is progressively added to copper sulphate solutions containing sodium tartrate in the ratio of 1 : 4·6 (see above), two series of titrations were carried out in which the complex tartrate solutions were buffered by the substitution for alkali of either borax or a mixture of disodium hydrogen phosphate and sodium hydroxide. Details of these titrations are given in Table II and typical titration curves are shown in the figure, curve No. 4 being that of solutions given in l. 3 of Table II and No. 5 that of solutions given in l. 6. Table II shows that a considerably larger proportion of phenol is obtained, *viz.*, 72·5—74·5% and 68·5—72·5% respectively. The titration curves reveal that, although well-defined inflexions were produced, the actual potentials set up were less negative than those established when alkali only was present.

TABLE II.

$CuSO_4$.	Concns. (mols./l.) of Na_2T.	$Na_2B_4O_7$.	Titre, c.c.	$\frac{CuSO_4}{NH_2 \cdot NHPh}$	$NH_2 \cdot NHPh$, %, converted into C_6H_6.	$C_6H_5 \cdot OH$.
0·010	0·046	0·10	2·9	3·45	27·5	72·5
0·015	0·069	0·15	4·3	3·48	26	74
0·025	0·115	0·25	7·15	3·49	25·5	74·5

$CuSO_4$.	Na_2T.	Na_2HPO_4.	NaOH.			
0·01	0·046	0·15	0·056	2·96	3·37	31·5	68·5
0·02	0·092	0·30	0·102	5·95	3·36	32	68
0·03	0·138	0·45	0·168	8·7	3·44	28	72

Influence of Complex Formation of Cupric Ions with (a) *Acetate Ion,* (b) *Carbonate Ion, on the Oxidising Action of Bivalent Copper.*—Some type of complex formation takes place between copper sulphate and sodium acetate or sodium carbonate, so much so that excess of either of these salts may be added to copper sulphate solution without causing precipitation despite the fact that the p_H at which basic copper salts are precipitated (p_H 5·4 at 18°) may be very much exceeded. At high temperatures (*e.g.*, 93°) some precipitation does occur from solutions to which sodium carbonate alone has been added; this, however, can be avoided by introduction of some bicarbonate with the carbonate.

TABLE III.

$CuSO_4$.	Concns. (mols./l.) of $CH_3 \cdot CO_2H$.	$CH_3 \cdot CO_2Na$.	Titre, c.c.	$\frac{CuSO_4}{NH_2 \cdot NHPh}$	$NH_2 \cdot NHPh$, %, converted into C_6H_6.	$C_6H_5 \cdot OH$.
0·02	0·2	0·2	10·0	2·00	100	—
0·025	5·0	5·0	11·0	2·27	86·5	13·5
0·025	0	5·0	11·0	2·27	86·5	13·5

$CuSO_4$.	$NaHCO_3$.	Na_2CO_3.				
0·01	0·675	0·675	4·3	2·32	84	16

The four titrations of 100 c.c. of solutions indicated in Table III were carried out at 93° with 0·1M-phenylhydrazine hydrochloride and their respective curves are Nos. 1, 2, 3, and 6.

The first titration in Table III is interesting in that it is the only one in which the phenylhydrazine is quantitatively oxidised to benzene. The titration curve (No. 1), however, shows that the completion of the reaction is not represented by a well-defined inflexion, but merely by an unsatisfactory "break." Curve No. 2 shows a small inflexion.

Discussion.—The curves show that the potentials of the platinum electrode, with respect to that of the normal calomel, set up during the initial and the final stages of the various titrations were largely influenced by the p_H values of the complex cupric salts being titrated. With the most alkaline tartrate solutions (Table I), an increase in the copper sulphate concentration from 0·01M to 0·15M causes an increase in the relative proportion of the benzene to the phenol produced. Lowering the p_H of the complex tartrate solution by means of either borax or sodium phosphate (Table II) reduces the amount of benzene as compared with phenol, whereas the reverse is true in the case of the low p_H complex acetate solutions and alkaline complex carbonate solutions. It was thought that these wide variations in the relative amounts of benzene and phenol might be accounted for by differences in the redox potentials corresponding to the complex copper solutions when compared with the potentials which would be acquired by the hydrogen electrode, assuming it to function reversibly, in the respective solutions. Such variations could only be established by large changes in the value of the ratio [Cu$^{\cdot}$]/[Cu$^{\cdot\cdot}$]. Calculation shows that, although differences do occur, they appear to be too small to explain the variations in the relative amounts of benzene and phenol formed in the course of these titrations. It was considered that a large redox potential would cause oxidation to proceed chiefly to phenol, whereas a small potential would cause it to proceed only as far as benzene.

Perhaps a more satisfactory way of considering this problem is to compare the initial titration potentials with those set up after the end-point has been passed. Curves Nos. 1 and 2 (complex acetate solutions) certainly reveal small differences between initial and final potentials; to a less extent, this is also shown by curve No. 3, and it is interesting that in these titrations the largest yields of benzene were produced. The batch of curves shown in the lower part of the figure, show that, whilst the final potentials assume tolerably constant values, the initial potentials become lower with increasing copper sulphate concentration, and it is very probable that it was these smaller differences which led to the increasingly greater proportions of phenylhydrazine being oxidised to benzene.

Britton and Königstein (J., 1940, 673) advanced evidence to support the view that potentiometric titrations of complex bivalent copper solutions, unlike other " redox " titrations, were made possible by the two successive reactions (i) $Cu^{\cdot\cdot} \longrightarrow Cu^{\cdot} + F$ and (ii) $Cu^{\cdot} \longrightarrow Cu + F$, equilibria involving (i) and (ii) being responsible respectively for the potentials in the initial and the final section of the graph. It is well known that copper may be deposited in the form of a mirror or else in a finely divided state from complex copper tartrate solution to which an excess of phenylhydrazine has been added. Although large excesses of phenylhydrazine were never added in these titrations, copper deposits were occasionally clearly visible on the electrodes.

Further evidence in support of this view is forthcoming from the final potentials observed in the titrations. They have the added advantage that they refer to solutions having p_H values extending over a wide range. It follows from the method of calculation adopted by Britton and Königstein (*loc. cit.*, p. 675) that the potential set up at a platinum electrode, E_{Pt} at 93°, corresponding to the equilibrium $Cu^{\cdot} \rightleftharpoons Cu$ is

$$E_{Pt} = \varepsilon_{Cu^{\cdot} \rightarrow Cu} - 0{\cdot}073 \log L_{CuOH}/[OH']$$
$$= \varepsilon_{Cu^{\cdot} \rightarrow Cu} - 0{\cdot}073 \log L_{CuOH} - 0{\cdot}073 \log K_w - 0{\cdot}073\, p_H$$

Assuming that $\varepsilon_{Cu^{\cdot} \rightarrow Cu}$ (0·52 volt at 18°, N-H = 0) and L_{CuOH} (approx. 10^{-14} at 18°) are not materially altered by increasing the temperature to 93°, and taking K_w to be equal to $10^{-12\cdot5}$ at 93°, we can calculate E_{Pt} for any p_H value, and consequently the potential of the platinum electrode against the normal calomel electrode can be computed, for Britton and Welford (J., 1937, 1846) have found that the potential of the latter (N-H = 0) at 91° is + 0·263 volt. Thus, in the complex tartrate titrations, the [OH′] varied from about 10^{-1} to almost 1M, and therefore the p_H ranged from 11·5 to 12·5. The potentials assumed by the platinum electrode should therefore fall within the range — 0·69 to — 0·76. The potentials corresponding to the final sections of the series of curves at the bottom of the figure show that this is the case.

The p_H in the complex tartrate–borax titration was approximately 8·8, and that in the tartrate–phosphate titration about 10·4. The final potential of the platinum electrode indicated in the former titration should be — 0·50 volt, which was actually observed, whereas in the latter case, it should be — 0·61 volt, which is slightly more negative than that found. In a similar way the potentials assumed by the platinum electrode at the end of the acetate titrations can be shown to depend on the reaction $Cu^{\cdot} \longrightarrow Cu$ and the effect which p_H has on the solubility product of cuprous hydroxide.

WASHINGTON SINGER LABORATORIES, UNIVERSITY COLLEGE, EXETER. [*Received, June 8th*, 1942.]

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101. *Optical Rotatory Dispersion of (—)Tetrahydrofurfuryl Alcohol.*

By RAYMOND S. AIRS, MICHAEL P. BALFE, MICHAEL IRWIN, and JOSEPH KENYON.

A two-term Drude equation is given which fits the rotatory dispersion of (—)tetrahydrofurfuryl alcohol recorded by Balfe, Irwin, and Kenyon (J., 1941, 312).

BALFE, IRWIN, and KENYON (*loc. cit.*) described the anomalous rotatory dispersion of (—)tetrahydrofurfuryl alcohol, but could not derive a Drude equation to fit the experimental results; they used seven-figure logarithms for the calculation. Working to ten figures with a calculating machine, we have now obtained a two-term

equation which fits the observations, and the calculation shows that at least eight figures are required for its solution.

The equation, for observed rotatory power in a 2-dm. column at 20°, is

$$\alpha_{\lambda}^{20°} = 42{\cdot}071/(\lambda^2 - 0{\cdot}03428) - 45{\cdot}917/(\lambda^2 - 0{\cdot}01712)$$

the characteristic frequencies being 1852 and 1308 A., indicating that both anisotropic centres in the molecules are associated with absorption bands of very low wave-length, in harmony with the formal saturation of the alcohol.

In the table, the observed rotatory powers are compared with those calculated from the above equation. The agreement is good, except for the observation at the lowest wave-length (3340 A.) where the curve has passed into the absorption band (absorption commenced at 3603 A.). From the equation, the following characteristics of the dispersion can be calculated (Lowry " Optical Rotatory Power," 1935, p. 139) :

Inflection at 7838 A. This is above the maximum wave-length at which observations were made.

Maximum at 6465 A. This is close to the maximum wave-length used, but the experimental results do indicate a maximum between 6200 and 6700 A.

Reversal of sign at 4711 A. The curve drawn through the experimental points crosses the axis of zero rotatory power at 4715 A.

[Observed rotatory powers in Roman type are from Table I of Balfe, Irwin, and Kenyon (*loc. cit.*), those in italics are from Table II; * indicates a numerical value taken from the rotatory powers of the (+)alcohol in Table II, and † indicates the four observations used as a basis for calculating the equation, except that at λ 6438, a value of −4·90° was taken, this being read from a smoothed curve through the experimental points.]

λ, A.	α, obs.	α, calc.	Diff.	λ, A.	α, obs.	α, calc.	Diff.	λ, A.	α, obs.	α, calc.	Diff.
6708	−4·70°	−4·87°	+0·17°	5461	3·95°†	3·95°	0·00°	4282	6·0°†	6·00°	0·00°
6438	4·97†	4·90	−0·07		*3·95*		0·00	4191	8·0	7·95	+0·05
	*4·85**		+0·05		*3·98**		−0·03	4108	10·0	10·04	−0·04
	4·87		+0·03	5086	2·72	2·60	−0·12	4032	12·0	12·25	−0·25
6104	4·59	4·81	+0·22		*2·60*		0·00	3978	14·0	14·02	−0·02
5893	4·54	4·67	+0·13		*2·64**		−0·04	3917	16·0	16·24	−0·24
	4·65		+0·02	4800	−0·96	−0·77	−0·19	3872	18·0	18·05	−0·05
	*4·64**		+0·03		*0·78**		−0·01	3767	23·0	22·93	+0·07
5780	4·47	4·54	+0·07	4603	+1·18	+1·13	+0·05	3669	28·0	28·51	−0·51
	4·44		+0·10	4529	2·0	2·02	−0·02	3603	33·0	32·92	+0·08
	*4·46**		+0·08	4384	4·0	4·14	−0·14	3392	52·0†	51·99	+0·01
				4358	*4·80*	4·58	+0·22	3340	60·0	58·20	+1·80
					*4·63**		+0·05				

We wish to thank Professor R. A. Fisher, F.R.S., who has provided facilities for the calculation.

BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, June 18th,* 1942.]

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102. *Sapogenins. Part XIII. The Position of the Double Bond in Acids of the β-Amyrin Group.*

By PHILIP BILHAM, GEORGE A. R. KON, and WALTER C. J. ROSS.

A new structural formula is put forward to explain the chemistry of the β-amyrin group of triterpenes.

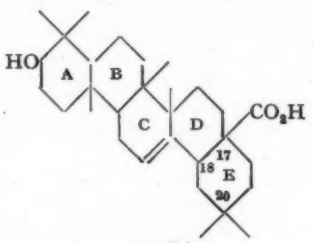
THE experiments described in the accompanying papers were primarily undertaken in continuation of the programme outlined in Part XII (this vol., p. 35), which had for its object the determination of the position of the carboxyl group in a number of sapogenins. It was thought desirable to include in this survey certain triterpene acids which are clearly related to the sapogenins, although they occur in the free state and not in the form of saponins. Such compounds are siaresinolic and sumaresinolic acid occurring in gum benzoin, and the acids of elemi resin.

Whilst the work on the acids of elemi resin described in Part XVI is still of a preliminary character, the investigation of glycyrrhetic acid (Part XIV) and siaresinolic acid (Part XV) has led to the almost complete elucidation of their constitution; and it soon became apparent that this could not be satisfactorily interpreted with the aid of the structural formulæ for the triterpenes which are current at the present time.

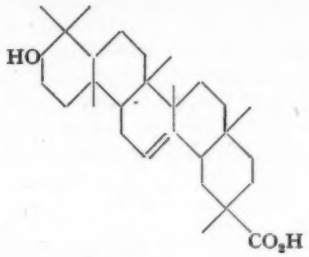
It has already been shown that the carboxyl group of oleanolic acid must occupy a position in one of the terminal rings of the hydropicene skeleton, leading to a modification of the current structural formula (I), in which this group was placed on C_{29} in ring E, but the remaining functional groups retained their original positions, as in (II) (Bilham and Kon, *Nature*, 1941, **147**, 745; J., 1941, 552).

It was foreseen at the time that the new formulation might give rise to difficulties, more especially as the formation of lactones from (II) appeared to require certain definite configurations of rings C, D, and E. The existence of two epimeric acids of the same formula, which is described in Part XIV, is possible according to this formula, but only one of these should be capable of lactone formation; a study of models shows that in the other form the carboxyl group is too remote from the unsaturated centre to allow interaction to take place.

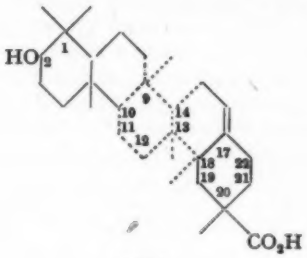
This, and other facts discovered in the course of the present work, have led us to consider afresh the position of the double bond in the acids of the β-amyrin group.



(I.)



(II.)



(III.)

Oleanolic acid being taken as typical, the requirements which have to be met are as follows : the unsaturated centre consists of a secondary and a tertiary carbon atom to allow the formation of a keto-lactone on oxidation, and there must be a methylene group next to it to account for the formation of αβ-unsaturated ketones, such as keto-oleanolic acid, thus :

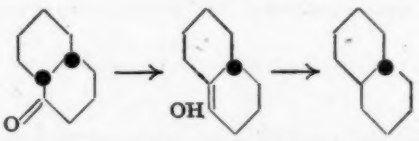
$$>C{:}CH{\cdot}CH_2— \quad \text{or} \quad —CH{:}C{\cdot}CH_2—$$

The task is simplified by the additional requirements, besides that already mentioned above, due to the new observations recorded in Parts XIV and XV which are that two methylene groups should be adjacent to the unsaturated centre. These represent the oxygen-bearing atoms of keto-oleanolic and of siaresinolic acid. Both these atoms are in proximity to the carboxyl group, as shown by the facilitation of hydrolysis of esters when either of the methylene groups is replaced by a carbonyl group. Neither of these groups can be situated in the same ring as the double bond, because when a double bond is introduced between them, this is conjugated with the double bond originally present and gives rise to selective absorption of light at a wave-length of *ca.* 2500 A., which is typical of a diene with conjugated double bonds distributed between two rings (compare, *e.g.*, Picard and Spring, J., 1941, 35). For the formulation of quillaic and echinocystic acid it is necessary that yet another methylene group, not identical with either of those already mentioned, should be situated next to the carbon atom bearing the carboxyl group. The unsaturated centre is thus part of the system

$$—CH{:}\underset{|}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CR(CO_2H){\cdot}CH_2—$$

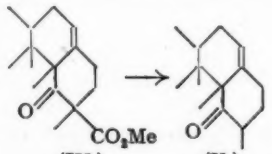
This has to be introduced into the 1 : 8-dimethylperhydropicene skeleton, which must be assumed to constitute the framework of the triterpene structure. It will be seen that, quite apart from the evidence of surface-film measurements which indicates the position of the carboxyl group in a terminal ring,* the only position in which the above system can be introduced is with the carboxyl group on C_{20} and the double bond in ring D. All the constituent atoms of ring E are thus accounted for, also a part of ring D. The parts of the molecule which had been completely elucidated by previous work included the whole of ring A and a part of ring B (the evidence for this has been fully summarised by Haworth, *Ann. Reports*, 1937, **34**, 327, and need not be recapitulated here; compare also the structure of bassic acid, J., 1940, 713); these have been embodied in formula (III) and shown in full lines. Our knowledge of the remainder of the molecule, which is shown in (III) by means of dotted lines, is derived from the dehydrogenation experiments of Ruzicka and his school (these also are summarised, *loc. cit.*); it includes ring C and three carbon atoms, assumed to belong to angular methyl groups, for which five positions are available. The arrangement shown in (III) is based on the isoprene hypothesis and the position of a methyl group on C_9 is retained from the older formulation. Another methyl group is placed on C_{13}, rather than on C_{14} as in the older formulæ (both arrangements are in agreement with the isoprene rule); the evidence for this is not yet complete and a discussion of it is reserved for a future communication, but it may be stated that such an arrangement appears to be required for the formulation of amyradienol I (Picard and Spring, *loc. cit.*), in which there are two double bonds in one ring, probably ring D.

The evidence for a methyl group on C_{18} is not conclusive, but it appears necessary in order to explain several characteristic features of quillaic and echinocystic acid. For instance, the existence of two series of mono- and di-ketones derived from echinocystic acid has been interpreted as due to stereoisomerism of the *cis-trans* α-decalone type (Bilham and Kon, J., 1940, 1469). The labile dextrorotatory ketones, *e.g.*, *iso*norechinostynenedione, pass into the stable lævorotatory compounds, such as norechinocystenedione, on treatment with alkali; a similar change is known to take place when *cis*-α-decalone is treated with alkali and is interpreted as involving enolisation towards the bridge head, for which the presence of a hydrogen atom is prerequisite :

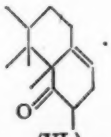


* It is hoped shortly to submit independent proof of this, based on purely chemical evidence.

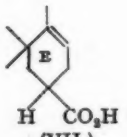
The new position for the double bond now put forward is not incompatible with stereoisomerism of this type, but it becomes necessary to explain why these ketones show no tendency to pass into their αβ-unsaturated isomerides as might be expected (compare James, Todd, and Noller, *J. Amer. Chem. Soc.*, **1939**, **61**, 2421); such a change occurs very readily in derivatives of siaresinolic acid (Part XV, p. 541). An angular methyl group on C_{18} affords a natural explanation of this difference, and also of the hydrolysis of the ketonic esters (partial structure IV) derived from quillaic and echinocystic acid with loss of the carbomethoxy-group (Elliott, Kon, and Soper, J., **1940**, **612**; Noller and White, *J. Amer. Chem. Soc.*, **1939**, **61**, **983**), giving ketones (V), in contrast to derivatives of siaresinolic acid. The carbonyl group in the former series of compounds can only enolise by displacement of the carbomethoxy-group, whereas in the latter an alternative mechanism is available.



(IV.) (V.)



(VI.)

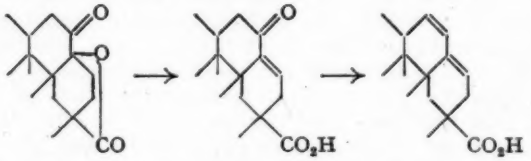


(VII.)

The precise nature of the isomerism between the two series of ketones still awaits an explanation; it may be due to the wandering of the double bond into ring E, in which case the marked lævorotation of the alkali-stable ketones of the partial structure (VI) would find a parallel in that of similarly constituted derivatives of siaresinolic acid.* An alternative explanation would be epimerisation about C_{20}, through the intermediate formation of an enol.

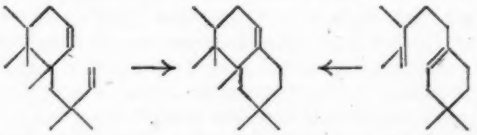
An apparent obstacle to the formulation discussed above is the decarboxylation of echinocystic acid with loss of water and formation of norechinocystadienol (Part XIV, p. 536); this must involve a retropinacolic change, in which case this compound should afford a valuable point of attack on the structural problem under discussion.

The formula (III) does not afford such an easy explanation of the results of dehydrogenation, notably of the formation of sapotalene (1 : 2 : 7-trimethylnaphthalene) from triterpenes, as the older formulation with a methyl group on C_{14}; it may, however, be pointed out that the mechanism by which this and other naphthalene derivatives are produced is in any case not fully understood. A cursory survey of the principal reactions of the triterpenes of the β-amyrin group shows that the new formula explains them adequately, with the possible exception of the experiments of Ruzicka, Cohen, and Sluys-Veer (*Helv. Chim. Acta*, **1939**, **22**, 350). For example, the formation of the *iso*-keto-acids, and of the dehydro-compounds derived from them, from keto-lactones (Kitasato, *Acta Phytochim.*, **1935**, **8**, 315) is readily formulated:



The structure of the isomeric keto-acids is discussed in Part XIV. It appears likely that β-oleananic acid, which is lævorotatory like the derivatives of siaresinolic acid with a double bond in ring E, may be represented by a structure analogous to that of the *iso*-keto-acid; the difference in the sign of rotation still remains to be explained.

Finally, the conversion of basseol into β-amyrin acetate (Beynon, Heilbron, and Spring, J., **1937**, 989), which constituted one of the difficulties of the older formulæ, can be pictured by one of the following schemes:



LABORATORIES OF J. LYONS AND CO., LTD., 149 HAMMERSMITH ROAD, LONDON, W.14.
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7.

[*Received, April 27th*, 1942.]

* A similar reversal of the sign of rotation takes place on decarboxylation of quinovic acid (Wieland, Schmitt, and Hrubesch, *Annalen*, **1939**, **539**, 219). Many reactions of the resulting pyroquinovic acid are in good agreement with the partial structure (VII).

103. *Sapogenins. Part XIV. The Constitution of Glycyrrhetic Acid and its Relation to Oleanolic Acid.*

By PHILIP BILHAM, GEORGE A. R. KON, and WALTER C. J. ROSS.

Glycyrrhetic acid has been converted into *deoxydeoxoglycyrrhetic acid*, unimolecular films of which have a limiting area of only 46 sq. A.; the carboxyl group in this acid must therefore be attached to a terminal ring of the hydropicene skeleton, namely, at C_{20} in ring E. The new acid is thus epimeric with γ-oleananic acid, and deoxoglycyrrhetic acid with oleanolic acid.

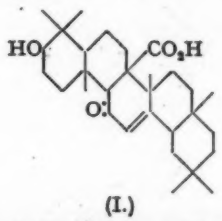
Acetylketo-oleanolic acid, which is known to be closely related to glycyrrhetic acid, has been pyrolysed and the resulting ketone, *oleadienone* II, reduced to *oleadienol* II. This alcohol gives unimolecular films of small area, indicating that the polar group, representing the carbonyl group of the parent acid, is situated in one of the end rings; this is to be expected on the basis of the formula (XIII) for the keto-acid, but is incompatible with formulæ based on the structure (II) previously assigned to oleanolic acid.

The dehydro-acid obtained by the reduction of keto-oleanolic acid (Kitasato, *Acta Phytochim.*, 1934—5, **8**, 1) is shown to be identical with the product obtained by the dehydration of methyl acetyloleanolate with selenium dioxide (Ruzicka, Grob, and Sluys-Veer, *Helv. Chim. Acta*, 1939, **22**, 788) and subsequent hydrolysis.

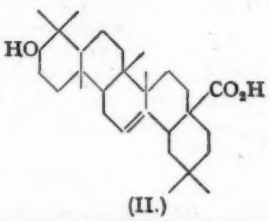
Glycyrrhetic acid has been similarly reduced to *dehydrodeoxoglycyrrhetic acid* (dehydro-*epi*oleanolic acid), the *methyl* ester of which has been acetylated to an *ester* identical with that obtained by the oxidation of acetyldeoxoglycyrrhetic ester with selenium dioxide. This dehydro-ester has an absorption spectrum indistinguishable from that of methyl acetyldehydro-oleanolate and of acetyldehydroamyrin (Picard and Spring, J., 1941, 35). There can be little doubt that all these compounds have a similar structure, from which it follows that the carbonyl group of glycyrrhetic acid occupies the same position as that of keto-oleanolic acid; these two compounds are regarded as the epimeric forms of the same structure (XIII).

GLYCYRRHETIC acid, the sapogenin of liquorice root, is probably the most interesting compound of those now examined because its constitution, already largely elucidated by Ruzicka and his collaborators, affords a test of the conclusions reached in the previous papers of this series regarding the position of the carboxyl group in triterpene acids of the β-amyrin group.

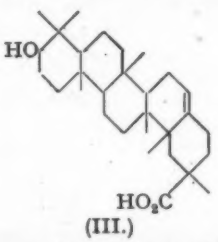
It is a hydroxy-keto-acid $C_{30}H_{46}O_4$; the carbonyl group is inert and the double bond occupies a position αβ with respect to it, giving rise to a characteristic absorption spectrum (Ruzicka, Leuenberger, and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1271). The carbonyl group is reduced to methylene by catalytic reduction and the resulting deoxoglycyrrhetic acid can be converted into β-amyrin (Ruzicka and Marxer, *ibid.*, 1939, **22**, 195). It follows from this that deoxoglycyrrhetic acid and oleanolic acid, which has been similarly converted into β-amyrin (Ruzicka and Schellenberg, *ibid.*, 1937, **20**, 1553), are identical except for the position of the carboxyl group, which is represented in β-amyrin by a methyl group. Taking into account its behaviour on dehydrogenation, and also the ready hydrolysis of glycyrrhetic esters, Ruzicka and Marxer formulate glycyrrhetic acid as (I), oleanolic acid being represented by (II).



(I.)



(II.)

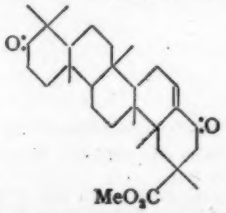


(III.)

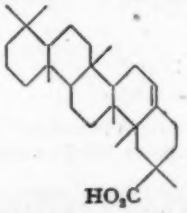
Bilham and Kon (*Nature*, 1941, **147**, 745; J., 1941, 552) have suggested that the carboxyl group of oleanolic acid should be placed on C_{20} in ring E, and a further revision of its constitution (preceding paper) leads to the structure (III).

Now it should be an easy matter to distinguish between a compound of the latter formula and one such as (I) by the surface-film method, after elimination of the hydroxyl and keto-groups: the structure with the carboxyl in the middle of the molecule will give films of large area of the order of 120 sq. A., with the molecule lying flat on the water surface, whereas one with the carboxyl group at one end of the molecule, like (III), will give films of comparatively small area.

Methyl glycyrrhetate, the starting point of our investigation, was prepared by the alcoholysis of commercial *glycyrrhizinum ammoniacale* (Voss, Klein, and Saher, *Ber.*, 1937, **70**, 122), and this was oxidised with chromic



(IV.)



(V.)

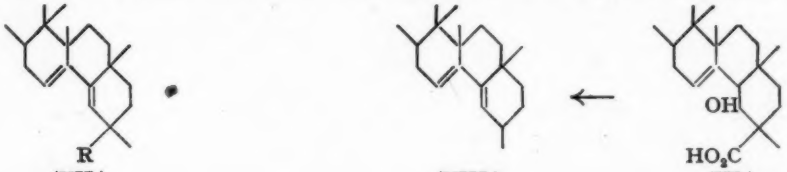
acid, giving the *diketo-ester*, m. p. 238—240°, which is now formulated as (IV). This compound had been obtained on a small scale by Bergmann and Bergmann (*Biochem. Z.*, 1933, **287**, 296) both by this method and

by the distillation of methyl glycyrrhetate with copper bronze, but its nature was apparently not realised. The diketo-ester is not reduced on heating with 50% hydrazine hydrate and sodium ethoxide, but undergoes hydrolysis and isomerisation; the *diketo-acid* still retains the system of conjugated double bonds originally present, as shown by its absorption spectrum, and is characterised by an *ester*, m. p. 232—234°, depressed by admixture of the original diketo-ester. The resistance of the carbonyl groups of the latter ester to reduction is only apparent and the diketo-ester is easily reduced by the Clemmensen method, giving *methyl deoxydeoxoglycyrrhetate*; this is hydrolysed by means of alkali under pressure to the *acid*, m. p. 303—306°, (V).

The acid forms solid films of good stability, withstanding a pressure of 14 dynes/cm. before collapse, and showing the phenomenon of spontaneous contraction. The value for the limiting area is 46 sq. A. and for μ 268 e.s.u. $\times 10^{-21}$; these constants are of the same order as those found for β- and γ-oleananic acids (Bilham and Kon, *loc. cit.*), hedraganic acid, ursanic acid, and dihydrobetulanic acid (Bilham, Kon, and Ross, this vol., p. 35). The small limiting area observed is incompatible with any formula such as (I) and suggests that in glycyrrhetic acid also the carboxyl group is situated in a terminal ring.

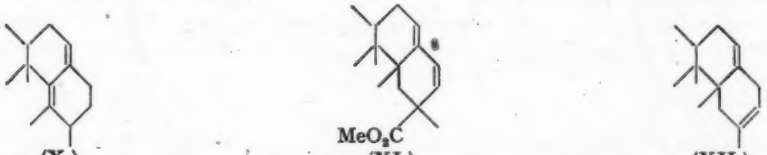
This cannot be ring A because glycyrrhetic acid is capable of forming a lactone (Ruzicka and Marxer, *loc. cit.*) and the carboxyl group must therefore be situated in reasonable proximity to the double bond. The only possible point of attachment for the carboxyl group becomes C_{20} in ring E, from which it follows that deoxydeoxoglycyrrhetic acid is epimeric with one of the oleananic acids (doubtless the γ-acid), and deoxoglycyrrhetic acid with oleanolic acid; the pairs of epimerides become identical when the carboxyl group is replaced by methyl.

It is hoped to obtain an independent proof of this important point by a chemical method, using a reaction which will destroy the configuration about C_{20}. One such reaction, analogous to the conversion of abietic acid into methyl abietin (Ruzicka, de Graaff, and Müller, *Helv. Chim. Acta*, 1932, **15**, 1300), is now being explored. An alternative method, though unsuccessful, has yielded results of some interest. Methyl acetyloleanolate gives on treatment with selenium dioxide a dehydro-ester, in which the new double bond is conjugated with that originally present, giving rise to an absorption spectrum with a maximum at 2500 A. (Ruzicka, Grob, and Sluys-Veer, *Helv. Chim. Acta*, 1939, **22**, 788).* The discoverers formulated this compound as having both double bonds in one ring, but there can be little doubt, from the position of the absorption maximum, that the double bonds must be distributed between two rings, as in the analogous compound derived from β-amyrin (Ruzicka, Müller, and Schellenberg, *ibid.*, p. 767). Dehydro-β-amyrin (amyradienol II) is formulated as (VII, R = Me) on the basis of the older structural formulæ (Picard and Spring, J., 1941, 35) and the dehydroester would then be (VII, R = CO_2Me). The elimination of the carbomethoxy-group from the latter compound will give rise to the compound (VIII), which should be identical with norechinocystadienol, recently obtained by Noller and Carson (*J. Amer. Chem. Soc.*, 1941, **63**, 2238) by the loss of carbon dioxide and water from echinocystic acid. The formation of this compound follows naturally from the formula (IX) put forward



(VII.) (VIII.) (IX.)

for echinocystic acid by Bilham and Kon (*loc. cit.*), and, in particular, the position of the second double bond. On the other hand, the new formulation (III) now adopted by us leads to the partial formula (X) for norechinocystadienol, the formation of which must involve a retropinacolic migration of an angular methyl group, whilst the dehydro-compounds formed with selenium dioxide will have the alternative structure (XI). A difference of structure is, indeed, made probable by an unmistakable difference in the absorption maxima: norechinocystadienol has a maximum at 2410 (Noller and Carson, *loc. cit.*, confirmed by us) or nearly 100 A. further from the visible end of the spectrum. Moreover, the spectra of the dehydro-dompounds have a distinct secondary maximum at *ca.* 2600 A. (see fig.).



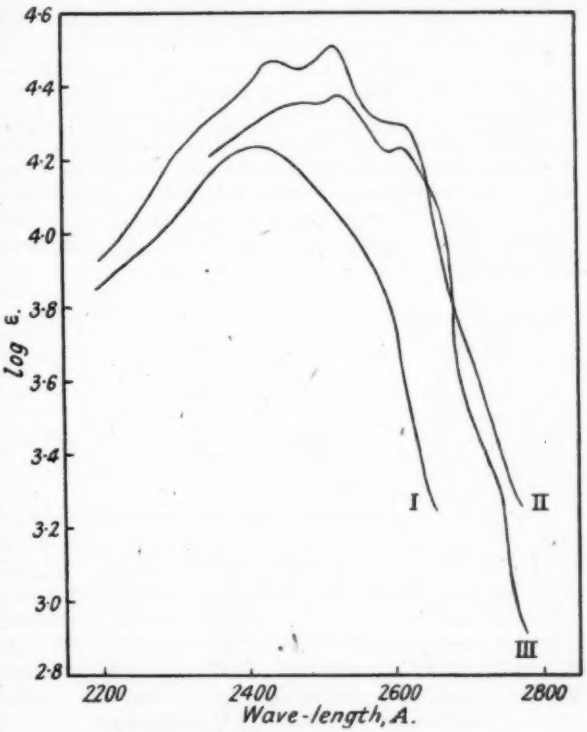
(X.) (XI.) (XII.)

The dehydro-ester, now represented by the partial formula (XI), is easily hydrolysed to the corresponding *hydroxy-acid*, which has a similar absorption spectrum, and loses carbon dioxide on heating. The product,

* A curious discrepancy has been noted between the results reported in this paper and our own observations: the acetyl dehydro-ester is described as having a rotation of + 137°, whereas the other compounds of this type are lævorotatory, and this point receives comment. It is now found that the rotation of the acetyl ester prepared by the selenium dioxide method is − 133°, and a specimen with $[\alpha]_D$ − 130° has also been obtained from siaresinolic acid (Part XV).

oleadienol I, is evidently formed with a simultaneous shift of a double bond because it is optically transparent; the presence of two double bonds is shown by its reaction with perbenzoic acid. Oleadienol I probably has the structure (XII); the movement of the double bond towards the α-carbon is the rule in the decarboxylation of βγ-mono-olefinic acids (compare, *e.g.*, the formation of methylene*cyclo*hexane from Δ¹-*cyclo*hexenylacetic acid; Wallach, *Annalen*, 1907, **353**, 287), but we are not aware of its occurrence in diolefinic acids.

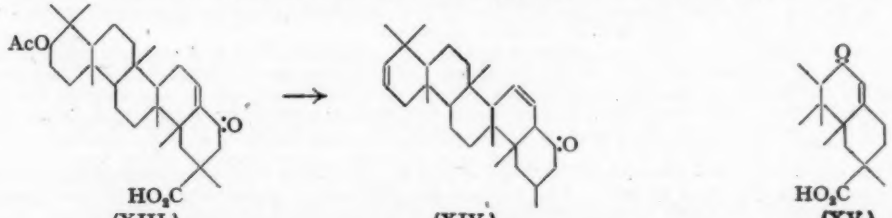
Now, if the movement of the double bond which destroys the original system of conjugated double bonds is correctly formulated above, it should be possible to obtain oleadienol I (XII) from glycyrrhetic acid. Methyl acetylglycyrrhetate is converted into the deoxo-ester (methyl acetyl*epi*oleanolate) by the Clemmensen method, which is simpler than the catalytic reduction originally used by Ruzicka, Leuenberger, and Schellenberg (*loc. cit.*) and gives an equally good yield. The deoxo-ester reacts with selenium dioxide to give a good yield of the *dehydro-ester*, which has an absorption spectrum indistinguishable from that of the ester (XI) (see fig.). The *hydroxy-dehydro-acid* is obtained from it on hydrolysis, but it does not lose the carboxyl group even on strong heating.



I. *Echinocystadienol.*
II. *Methyl acetyldehydrodeoxoglycyrrhetate.*
III. *Methyl acetyldehydro-oleanolate.*

A similar difficulty in removing the carboxyl group is experienced with deoxydeoxoglycyrrhetic acid and also with glycyrrhetic acid itself and appears to be characteristic of the whole series. This failure precluded the production of ketones (or alcohols) which could be used to determine the position of the carbonyl group of glycyrrhetic acid by the surface film method.

This has been successfully achieved with acetylketo-oleanolic acid. This acid is very similar to acetylglycyrrhetic acid; like the latter, it is an αβ-unsaturated ketone, it is produced by the oxidation of acetyloleanolic acid under the conditions used to convert acetyldeoxoglycyrrhetic acid into acetylglycyrrhetic acid (Ruzicka and Marxer, *loc. cit.*), and it has been suggested that the carbonyl group must occupy a similar position, β or γ with respect to the carboxyl, because the esters of glycyrrhetic and keto-oleanolic acids are equally readily hydrolysed (Ruzicka, Leuenberger, and Schellenberg, *loc. cit.*); in the light of the present work there is little doubt that these two acids are epimeric about C_{20} and are both represented by formula (XIII).



(XIII.) (XIV.) (XV.)

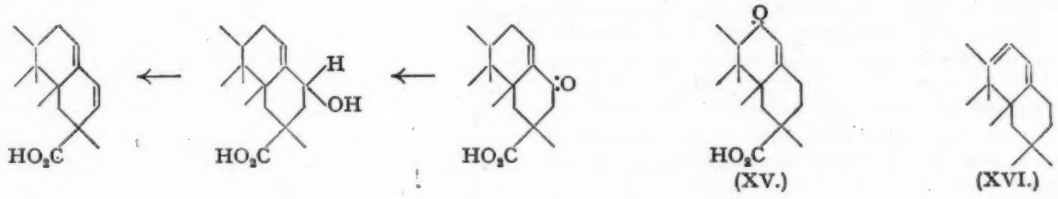
Acetylketo-oleanolic acid, on heating in a sealed tube, loses carbon dioxide and acetic acid (compare the formation of oleanylene II from acetyloleanolic acid; Kitasato, *Acta Phytochim.*, 1934—5, **8**, 207), forming *oleadienone II*. The change is evidently accompanied by the migration of a double bond because the ketone is optically transparent. It is probably represented by formula (XIV), although the position of the double bond cannot be regarded as certain.

The ketone does not form satisfactory films, but the *alcohol* obtained by reduction with sodium and alcohol (*oleadienol II*) gives solid films with a limiting area of 41 sq. A., which is the smallest area yet observed in a triterpene derivative; μ is 117 e.s.u. × 10^{-21}. This clearly indicates that the hydroxyl group, derived from the carbonyl group of acetylketo-oleanolic acid, occupies a position in one of the end rings of the polycyclic system; it appears to exclude a position in ring D, which could be derived from formula (III) by placing the carbonyl group as in the partial formula (XV).

The decarboxylation of acetylketo-oleanolic acid has already been carried out by boiling with quinoline, an acetoxyketone with an additional double bond being obtained (Ruzicka, Cohen, Furter, and Sluys-Veer, *Helv. Chim. Acta*, 1938, **21**, 1735). It was hoped that this compound would prove useful in the elucidation of

the structure of the dehydro-compounds. The *compound* obtained, however, melted higher than the required ketone and differed from it in being optically transparent; it is clear that the elimination of the carboxyl group had been accompanied by the movement of the double bond, destroying the conjugated system originally present, just as in the formation of oleadienone II, and a new double bond had not been introduced. The new ketone is evidently the 2-*acetoxy*-compound corresponding to oleadienone II.

Whilst it has not proved possible to obtain analogous compounds from glycyrrhetic acid owing to its resistance to decarboxylation, proof of the complete analogy in structure of this acid and keto-oleanolic acid was obtained by the following reactions: keto-oleanolic acid was reduced with sodium in alcoholic solution to the dehydro-acid, which is doubtless identical with the dehydro-acid already obtained by means of sodium amalgam reduction by Kitasato (*Acta Phytochim.*, 1934—5, **8**, 1; *loc. cit.*). This acid has also been found to be identical with the dehydro-oleanolic acid (XI) prepared by the selenium dioxide process, which has already been discussed above; the formation of it follows naturally from the formula (XIII) for the keto-acid, but would be difficult to interpret on the basis of the structure (XV); it also affords conclusive evidence of the position of the double bond adopted in that formula as against a position in the middle of the molecule, as in (II).



(XV.) (XVI.)

Glycyrrhetic acid was similarly reduced and gave a diene-acid which was isolated in the form of its *methyl* ester; the *acetyl* derivative of this proved to be identical with the acetyl dehydro-ester obtained by the selenium dioxide oxidation of deoxoglycyrrhetic ester. The behaviour of glycyrrhetic acid in this reaction is thus an exact parallel to that of keto-oleanolic acid and leaves little room for doubt that their structures are similar.

The formation of the diene acids from keto-oleanolic and glycyrrhetic acid described above is also analogous to the formation of dehydro-β-amyrin (amyradienol II) from keto-β-amyrin (Picard and Spring, *loc. cit.*) and appears to afford a proof that the double bond and the keto-group in all these compounds must be situated in different rings. The formation of the isomeric compound with two double bonds in one ring (amyradienol I), which is probably represented by the structure (XVI), still awaits a satisfactory explanation.

Experimental.

M. p.'s were determined in sealed capillaries and are uncorrected; unless otherwise stated, analysis specimens were dried for 2 hours at 100°/1—2 mm.; rotations were determined in chloroform solution; the technique of surface-film measurements was that described in Part XI (J., 1941, 552).

Methyl Glycyrrhetate.—50 G. of *Glycyrrhizinum ammoniacale* (British Drug Houses Ltd.) were refluxed with 300 c.c. of 3% methyl-alcoholic hydrogen chloride, the solution evaporated to dryness under reduced pressure, the residue extracted with ether, and the dark extract passed through a long column of activated alumina, on which a deep yellow band formed near the top. The methyl ester, m. p. 222—224°, was recovered from the filtrate and crystallised by solution in warm acetone and addition of water until a turbidity appeared.

Diketo-ester (V).—4·25 G. of methyl glycyrrhetate in 116 c.c. of AnalaR acetic acid were gradually treated with 12·3 c.c. of Kiliani's chromic acid solution at room temperature. After ½ hour methyl alcohol was added, and the solution warmed to destroy the excess of reagent, then diluted with its own volume of water. On cooling, the new *ester* (60% yield) crystallised; if more water was added to precipitate the product completely, a gum was obtained. The diketo-ester crystallised from methyl alcohol in plates, m. p. 238—240° (Found: C, 76·8; H, 9·5. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%).

500 Mg. of the diketo-ester were heated for 12 hours with 2·25 c.c. of 50% hydrazine hydrate and 400 mg. of sodium in 8 c.c. of alcohol in a sealed tube at 200°. The product was diluted (no precipitate formed at this stage), acidified, and extracted with ether. The *acid* crystallised from methyl alcohol and melted at 325° (Found: C, 77·1; H, 9·5. $C_{30}H_{44}O_4$ requires C, 76·9; H, 9·5%); the light absorption in ethyl alcohol showed a band with a maximum at 2440, $\log \epsilon_{max.}$ 4·20; it was re-esterified with diazomethane and gave a *methyl* ester, m. p. 245—247° after crystallisation from methyl alcohol, depressed by admixture of the original diketo-ester (Found: C, 77·5; H, 9·6. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%).

Deoxydeoxoglycyrrhetic Acid.—1·3 G. of the diketo-ester were boiled for ½ hour with 140 c.c. of acetic acid, 35 c.c. of hydrochloric acid, and 60 g. of amalgamated zinc. The solution was diluted and extracted with light petroleum (b. p. 60—80°), the extract being percolated through a 15 cm. column of activated alumina, which was then washed with the pure solvent until no more crystalline material was eluted (yield, 520 mg.); the *methyl* ester formed sparkling plates, m. p. 182°, after two crystallisations from methyl alcohol (Found: C, 81·7; H, 11·2. $C_{31}H_{50}O_2$ requires C, 82·0; H, 11·2%). 520 Mg. of the ester were heated for 4 hours with 52 c.c. of 20% potassium hydroxide in 85% alcohol in two sealed tubes at 170°. The product was diluted, acidified, and extracted with ether, the acid re-extracted by repeated shaking with 10% sodium hydroxide solution, and the alkaline extract acidified and extracted with ether. The *acid* crystallised in contact with methyl alcohol and was recrystallised by solution in acetone–ether and evaporation of the ether; it formed iridescent plates, m. p. 303—305° (Found: C, 82·1; H, 10·9. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

Methyl Acetyldeoxyglycyrrhetate.—Crude methyl glycyrrhetate (13 g.) was boiled with 130 c.c. of acetic anhydride and 1 g. of fused sodium acetate for an hour, and the solution then gradually diluted with water, giving 3·7 g. of crystalline acetyl ester, m. p. above 280°; a little more could be recovered by further dilution of the mother-liquor.

The acetyl ester was reduced by the Clemmensen method as described above, only half the amounts of reagents being used; the product, purified in the same way and crystallised from acetone, had m. p. 254—255°, depressed by the starting material (lit., 265° corr.).

Methyl Acetyldehydrodeoxoglycyrrhetate.—1·25 G. of the above ester were boiled for 48 hours with 75 c.c. of acetic acid and 0·6 g. of selenium dioxide. The solution was evaporated to dryness under reduced pressure, the residue extracted with ether, and the solution filtered from selenium and again evaporated to dryness. The residue was dissolved in benzene and percolated through a short column of activated alumina. The recovered *ester* crystallised from chloroform–methyl alcohol in iridescent plates (600 mg.), m. p. 230—231°, $[\alpha]_D$ − 32° (c = 0·73) (Found: C, 77·9; H, 9·9. $C_{33}H_{50}O_4$ requires C, 77·6; H, 9·8%).

Dehydrodeoxoglycyrrhetic Acid.—The above acetyl ester was hydrolysed as described on p. 538. The *acid* formed needles from acetone, m. p. above 305° (Found: C, 79·5; H, 10·1. $C_{30}H_{46}O_3$ requires C, 79·3; H, 10·1%). All attempts to remove the carboxyl group of this acid by heating alone or with quinoline and copper powder were unsuccessful.

The same acid was also obtained when a boiling solution of glycyrrhetic acid in 200 vols. of alcohol was gradually saturated with sodium. The oily acid recovered by dilution, acidification, and extraction with ether crystallised in contact with methyl alcohol. It was esterified with diazomethane; the *methyl* ester formed small plates, m. p. 262—263° after two crystallisations from methyl alcohol, and gave a brown colour with tetranitromethane in chloroform (Found: C, 79·3; H, 10·5. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%). For identification the ester was dissolved in 20 parts of warm pyridine–acetic anhydride (1 : 1) and left at room temperature. After some hours the characteristic iridescent plates of the acetyl ester began to separate. Water was added, and the precipitated ester crystallised once from methyl alcohol. It had m. p. 229—230°, not depressed by the ester obtained as above.

Bromination of Methyl Acetylglycyrrhetate.—Methyl acetylglycyrrhetate (220 mg.) in 6·6 c.c. of acetic acid was kept at 85—95° while 2·35 c.c. of 3% bromine in acetic acid were added dropwise. The solid which separated on cooling was recrystallised from methyl alcohol, giving long needles, m. p. 210—215°. It contained halogen and was not the expected dehydro-compound. Attempts to debrominate it did not lead to crystalline products.

Dehydro-oleanolic Acid.—(1) Methyl acetyldehydro-oleanolate was prepared as described by Ruzicka, Grob, and Sluys-Veer (*loc. cit.*; compare also above). The acetyl ester had m. p. 225°, $[\alpha]_D$ − 133° (c = 1·53) (absorption spectrum in the fig.); it was hydrolysed under pressure as described above. The *hydroxy-acid* crystallised from methyl alcohol in hexagonal plates, m. p. 274—275° (Found: C, 79·0; H, 10·3. $C_{30}H_{46}O_3$ requires C, 79·3; H, 10·1%). (2) Keto-oleanolic acid (see below) was reduced with sodium and alcohol exactly as described above. The acid recovered had m. p. 270—271°, not depressed by the acid prepared by method (1); it gave an ester, m. p. 164°, not depressed by the ester, m. p. 166—167°, prepared by mild hydrolysis of the acetyl ester obtained by method (1) (compare Ruzicka *et al.*, *loc. cit.*).

Oleadienol I.—The dehydro-acid was heated until it was just melted, dissolved in ether, freed from acid by shaking with alkali, and the ether evaporated. The residue was repeatedly crystallised from methyl alcohol, the m. p. gradually rising to 218—219°. The *compound* evidently contained methyl alcohol of crystallisation (compare norechinocystadienol; Noller and Carson, *loc. cit.*, and this paper), $[\alpha]_D$ + 97° (c = 2·19 in dioxan) (Found: C, 81·5, 81·8; H, 11·7, 11·2. $C_{29}H_{46}O,CH_4O$ requires C, 81·4; H, 11·3%). The substance was purified by chromatographic adsorption from a benzene solution, but its properties were not appreciably changed. Titration with perbenzoic acid indicated 1·85 double bonds, a specimen of oleanolic acid titrated at the same time showing 0·8 double bond. It was recovered unchanged after an alcoholic solution had been shaken with hydrogen and Adams's catalyst. The acetate prepared by means of acetic anhydride and pyridine in the cold crystallised from methyl alcohol in needles, m. p. 186—188°, $[\alpha]_D$ + 87° (c = 1·74 in dioxan).

Acetylketo-oleanolic Acid. The oxidation of acetyloleanolic acid was carried out according to Ruzicka, Cohen, Furter, and Sluys-Veer (*loc. cit.*). The acid recovered from the sodium salt and crystallised from methyl alcohol–ether had m. p. 288° (lit., 282—284° corr.), together with a more soluble fraction, m. p. 264°; the latter also had the characteristic absorption of an $\alpha\beta$-unsaturated ketone with a maximum at 2510 A., log $\varepsilon_{max.}$ 4·1.

Decarboxylation. The acid, m. p. 288°, was decarboxylated in boiling quinoline as described by Ruzicka *et al.* (*loc. cit.*). The *product* was crystallised from methyl alcohol; it sintered at 222°, but did not melt completely until 235—240°, and gave a yellow colour with tetranitromethane (Found: C, 79·6; H, 10·3. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%). The same product, evidently an acetoxy-ketone, was also obtained from the lower-melting specimen of the keto-acid. A small amount of the acetoxy-ketone was reduced with 90% hydrazine hydrate and sodium ethoxide as described on p. 538; the resulting compound crystallised from methyl alcohol in needles, m. p. 217—219°, depressed by oleanol (m. p. 220—222°).

Oleadienone II.—Acetylketo-oleanolic acid was kept in a sealed Pyrex tube at 340° for an hour (nitrate bath). *Oleadienone II* crystallised from methyl or ethyl alcohol in pearly plates, m. p. 209—210°, raised to 210—212° by a final crystallisation from light petroleum (b. p. 60—80°); it gave a yellow colour with tetranitromethane (Found: C, 85·2; H, 10·8. $C_{29}H_{44}O$ requires C, 85·3; H, 10·9%).

Oleadienol II.—The ketone was reduced with sodium and alcohol as described above. The *alcohol*, crystallised from methyl alcohol and finally from light petroleum, formed needles, m. p. 219—221° (Found: C, 84·7; H, 11·5. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3%).

Norechinocystadienol.—Our preparation of this compound was completed before the appearance of the paper by Noller and Carson (*loc. cit.*) and our results agree well with theirs. The highest m. p. observed by us was 191°; we were unable to obtain good analytical figures for the pure compound, but the product containing methyl alcohol of crystallisation was satisfactorily analysed (Found: C, 81·7, 81·8; H, 11·1, 10·9. $C_{29}H_{46}O,CH_4O$ requires C, 81·4; H, 11·3%). The *acetate* formed plates from methyl alcohol, m. p. 175—177°, $[\alpha]_D$ + 46° (c = 1·63 in dioxan) (Found: C, 82·1; H, 10·9. $C_{31}H_{48}O_2$ requires C, 82·2; H, 10·7%).

The authors' thanks are due to Dr. R. H. Kerlogue for the absorption spectra, to the Royal Society for a grant, and to Messrs. Whiffen and Sons, Ltd., for a gift of residues from the manufacture of clove oil.

Laboratories of J. Lyons and Co., Ltd., 149 Hammersmith Road, London, W.14.
Imperial College of Science and Technology, London, S.W.7.

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104. *Sapogenins. Part XV. Siaresinolic Acid.*

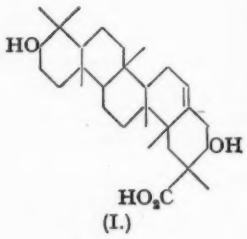
By Philip Bilham, George A. R. Kon, and Walter C. J. Ross.

Siaresinolic acid is shown to belong to the β-amyrin group of triterpene acids by its conversion into oleanene III, a hydrocarbon obtained from oleanolic acid by Winterstein and Stein (*Annalen*, 1933, **502**, 223). One hydroxyl group of siaresinolic acid occupies a position at C_3 in ring A; the second hydroxyl is attached to C_{21} in the other terminal ring, E, as shown by measurements of unimolecular films of *dihydronorsiaresinol*. The double bond of siaresinolic acid is situated in the βγ-position with respect to the carbon atom carrying this group; it is also shown to occupy the same position as the double bond of oleanolic acid by the dehydration of *methyl 2-acetylsiaresinolate* to methyl acetyldehydro-oleanolate. This also shows that, apart from the additional hydroxyl at C_{21}, siaresinolic acid is identical with oleanolic acid.

The reactions of siaresinolic acid cannot be satisfactorily interpreted on the basis of the older formulæ for the compounds of the β-amyrin group, but support the new structure put forward in Part XIII (this vol., p. 533).

Siaresinolic acid, which occurs in Siamese gum benzoin, has the formula $C_{30}H_{48}O_4$ (Zinke and Lieb, *Monatsh.*, 1918, **39**, 95, 627). On dehydrogenation with selenium it gives most of the products obtainable from triterpenes, notably 1 : 8-dimethylpicene, sapotalene, and hydroxyagathalene (2-hydroxy-1 : 5 : 6-trimethylnaphthalene) (Ruzicka, Brüngger, Egli, Ehmann, Furter, and Hösli, *Helv. Chim. Acta*, 1932, **15**, 431; Ruzicka, Brüngger, Egli, Ehmann, and Goldberg, *ibid.*, p. 1496), from which it follows that the acid must have a skeleton based on 1 : 8-dimethylpicene, and that, like oleanolic acid, it has a hydroxyl group at C_3 in ring A. Moreover, the formation of a bromo-lactone on treatment of the acid with bromine (Winterstein and Egli, *Z. physiol. Chem.*, 1931, **202**, 207) shows that it is a βγ-, γδ- or δε-unsaturated acid and suggests a similarity in structure with the acids of the β-amyrin group. The experiments described below lead to the conclusion that siaresinolic acid is 21-hydroxyoleanolic acid and is represented by the formula (I).

Siaresinolic acid has two hydroxyl groups, as shown by determinations of active hydrogen (Winterstein and Egli, *loc. cit.*), but these are of unequal reactivity, like those of echinocystic acid (compare Bergsteinsson and Noller, *J. Amer. Chem. Soc.*, 1934, **56**, 1403). The acid forms a monobenzoate (Zinke and Lieb, *loc. cit.*) and a monoacetate (Winterstein and Egli, *loc. cit.*); the methyl ester similarly gives a *monoacetyl* derivative, whereas the second hydroxyl group does not react. The more reactive hydroxyl group, which may be designated as $OH^{(1)}$, is doubtless that attached to C_3, since a hydroxyl group in that position is known to be reactive; separate proof of this is given on p. 541. The less reactive hydroxyl group, $OH^{(2)}$, is secondary and can be oxidised; *e.g.*, the monoacetyl ester mentioned above gives the *acetate* of a *ketohydroxy-ester* (methyl 21-keto-oleanolate), $C_{33}H_{50}O_5$, on treatment with chromic acid.



(I.)

The position of the hydroxyl $OH^{(2)}$ in proximity to the carboxyl group follows from the observation that, although methyl siaresinolate resists hydrolysis even under very vigorous conditions, and the carbomethoxyl group therefore occupies a sterically protected position, hydrolysis becomes easy once $OH^{(2)}$ has been oxidised. The above acetylketo-hydroxy-ester at once develops a strong yellow colour with alkali and undergoes rapid hydrolysis. Similarly, *methyl siaresinonate*, the diketo-ester obtained by the oxidation of methyl siaresinolate with chromic acid, is also easily hydrolysed. In this respect these esters resemble the diketo-esters derived from echinocystic acid (Noller and White, *J. Amer. Chem. Soc.*, 1939, **61**, 983) and from quillaic acid (Elliott, Kon, and Soper, J., 1940, 612). The diketo-ester is evidently capable of enolisation, because, apart from the yellow colour which it develops with alkali, it liberates one molecule of methane under the conditions of the Zerevitinov test. The diketo-ester derived from echinocystic acid also has been found to behave in this way by Noller and White (*loc. cit.*; confirmed by Carson and Noller, *ibid.*, 1941, **63**, 621), although under the conditions used in our Microanalytical Department (*iso*-amyl ether as solvent, room temperature) this was not observed (Elliott, Kon, and Soper, *loc. cit.*); it may be safely inferred that methyl siaresinonate is appreciably more acidic than the isomeric compound.

An important difference lies in the fact that the ketonic acids formed by the hydrolysis of siaresinonic ester and of the acetoxy-keto-ester do not lose carbon dioxide with the production of ketones, but are isolated as such, although they are readily decarboxylated. In spite of their apparent stability they are formulated as β-ketonic esters (see p. 542).

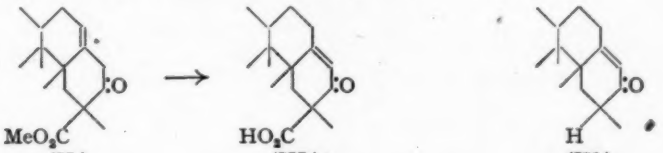
When methyl siaresinonate is reduced by the Clemmensen method, only one carbonyl group, namely that at C_3, is attacked, and the ester undergoes hydrogenation at the same time; the product, *methyl-2-deoxo-dihydrosiaresinonate*, no longer gives a colour with tetranitromethane. The formation of hydrogenation products in the course of the Clemmensen reaction has been noted in certain alkaloid derivatives (Awe and Unger, *Ber.*, 1937, **70**, 472) and another case is reported in Part XVI (this vol., p. 546). The carbonyl group which escapes reduction must be that derived from $OH^{(2)}$, because the new ester also is readily hydrolysed.

The same carbonyl group resists reduction when methyl siaresinonate is heated with hydrazine hydrate and sodium ethoxide. The product is *β-2-deoxosiaresinonic acid*. The apparent resistance to reduction of the carbonyl group in this and other similar cases is probably due to a tendency to enolisation rather than the effect of steric hindrance, and has also been encountered in derivatives of glycyrrhetic acid.

β-Deoxosiaresinonic acid is converted on melting into *norsiaresinone*, a ketone $C_{29}H_{46}O$ (IV). This com-

pound also resists reduction by the hydrazine method; the carbonyl group is, however, easily reduced by the Clemmensen method with the formation of a hydrocarbon, which has been identified as oleanene III by its m. p., mixed m. p., and rotation. Oleanene III has previously been obtained from oleanolic acid (Winterstein and Stein, *Annalen*, 1933, **502**, 222) and from echinocystic acid (Todd, Harris, and Noller, *J. Amer. Chem. Soc.*, 1940, **62**, 1624) and its formation shows that siaresinolic acid must have the carbon skeleton common to these triterpenes. In particular, it may be inferred that the carboxyl group is similarly situated in ring E (compare Bilham and Kon, J., 1941, 552); the position of the double bond cannot be inferred from this, because oleanene III is probably a secondary product formed by the movement of the double bond from its original position.

It can, however, be shown that the double bond of siaresinolic acid is situated in a $\beta\gamma$-position with respect to the carbon atom carrying $OH^{(2)}$. Methyl siaresinonate (II), which is optically transparent, is hydrolysed to β-*siaresinonic acid* (III) and this is re-esterified with diazomethane to a β-ester isomeric with the starting material; the latter is therefore designated as the α-ester. The β-ester shows selective absorption of light with a maximum at 2510 A., having an intensity $\log \varepsilon_{max.} = 3{\cdot}95$.



The isomerisation of the α- to the β-compound is evidently due to the wandering of the double bond in the course of alkaline hydrolysis, with the formation of a conjugated system. A similar change is observed when the acetoxy-keto-ester previously mentioned is hydrolysed; the product is the β-*hydroxyketo-acid*, which is re-esterified to a strongly lævorotatory β-*ester* (light absorption: maximum at 2520 A., $\log \varepsilon_{max.} = 3{\cdot}99$) and this is oxidised by chromic acid to methyl β-siaresinonate. The hydroxy-keto-ester is isomeric with methyl 22-keto-oleanolate and methyl glycyrrhetate (compare preceding paper), but differs from them in rotation.

β-Deoxosiaresinonic acid, which has already been described, gives a *methyl* ester having a spectrum with a maximum at 2510 A., $\log \varepsilon_{max.} = 4{\cdot}02$; on the other hand, the saturated deoxo-dihydro-ester formed by the Clemmensen reduction of methyl α-siaresinonate is hydrolysed without isomerisation, as would be expected. The acid so formed is re-esterified to a dextro-rotatory ester identical with the starting material.

The movement of the double bond in derivatives of siaresinonic acid is accompanied by remarkably large changes of optical rotation; the compounds of the α-series, with the double bond in the original position, have positive rotations of the order of + 130°. The compounds of the β-series, with the double bond in the αβ-position with respect to the carbonyl group, are strongly lævorotatory, with $[\alpha]_D$ of the order of − 200° or more. It seems hardly possible that such large changes would have been observed if the isomerisation from the α- to the β-series had been incomplete, as might be inferred from the somewhat low intensities of the absorption spectra; these appear to be due to some constitutive influence, such as is observed, for example, in 3-hydroxy-6-keto-Δ^4-cholestene (Heilbron, Jones, and Spring, J., 1937, 801), Δ^4-androstene-6 : 7-dione (Ruzicka, Grob, and Raschka, *Helv. Chim. Acta*, 1940, **23**, 1518), and Δ^1-steroids (Butenandt, Mamoli, Dannenberg, Masch, and Paland, *Ber.*, 1939, **72**, 1617; see also Inhoffen and Huang-Minlon, *ibid.*, 1938, **71**, 1720; Barnett and Reichstein, *Helv. Chim. Acta*, 1938, **21**, 926).

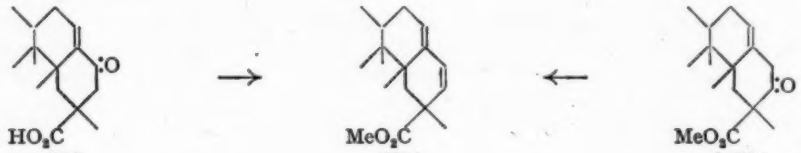
It might have been expected that methyl siaresinolate would undergo oxidation by the Oppenauer reagent, which is generally regarded as specific for $\beta\gamma$-unsaturated alcohols. The ester does indeed undergo oxidation when treated with aluminium *tert.*-butoxide and *cyclo*hexanone, but the *ester*, $C_{31}H_{48}O_4$, which is produced shows no selective absorption of light in the expected region of the spectrum. The oxidation thus either involves the hydroxyl group at C_3, or $OH^{(2)}$ is oxidised without movement of the double bond.

Methyl monoacetylsiaresinolate is dehydrated on boiling with phosphoric oxide in benzene solution, yielding methyl acetyldehydro-oleanolate, identical with the product obtained by the action of selenium dioxide on methyl acetyloleanolate (Ruzicka, Grob, and Sluys-Veer, *Helv. Chim. Acta*, 1939, **22**, 788), as shown by its m. p., mixed m. p., rotation and absorption spectrum. This shows that the skeleton of siaresinolic acid must be identical with that of oleanolic acid, except for the additional hydroxyl group $OH^{(2)}$ in the former acid, and in particular, that the position of the double bond must be the same. Since this is situated in a $\beta\gamma$-position with respect to the carbon atom carrying $OH^{(2)}$, the latter would be placed at C_{21} on the basis of the new formula for oleanolic acid (Part XIII; this vol., p. 533).

Decisive evidence as to the position of $OH^{(2)}$ in the molecule is also afforded by surface-film measurements. Norsiaresinone forms a very weak, unstable film, which appears to have a small limiting area of the order of 47 sq. A. On reduction with sodium and alcohol the ketone is converted into the saturated alcohol, *dihydronorsiaresinol*; this is to be expected since norsiaresinone is an αβ-unsaturated ketone as shown by its absorption spectrum (maximum at 2490 A., $\log \varepsilon_{max}$ 3·97). The new alcohol forms films of good stability, which do not exhibit spontaneous contraction and have a limiting area of 43·5 sq. A., with $\mu = 171$ e.s.u. $\times 10^{-31}$. Such a limiting area is only compatible with a position of the polar group in a terminal ring, and since the alternative

positions in ring A are excluded, it can only be attached to C_{21} or C_{22}. In agreement with this, methyl 2-deoxodihydrosiaresinonate has a limiting area of 65 sq. A. and $\mu = 872$ e.s.u. $\times 10^{-21}$. These results are in complete accord with the formulation deduced from purely chemical considerations.

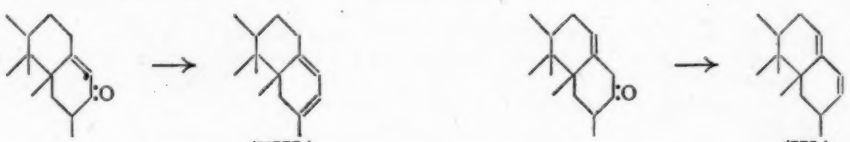
Now the dehydro-ester (VI) mentioned above has also been obtained from keto-oleanolic acid (V), the acetyl ester of which is isomeric, and not identical, with the acetyl-keto-ester (VII) described on p. 540; the former is an αβ- and the latter a βγ-unsaturated ketone. The double bond must occupy the same position in both compounds and they differ by the position of the carbonyl group, which must, however, be placed in a terminal ring in both compounds :



(V.) (VI.) (VII.)

It follows from this that the two carbonyl groups of (V) and (VII) severally represent two methylene groups of oleanolic acid, which are situated in proximity to the carboxyl group and in a different ring from that which houses the double bond.

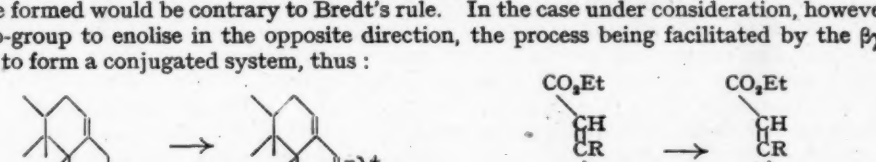
Certain by-products isolated in the reduction of norsiaresinone are of interest. One of these is a *diene* with a system of conjugated double bonds, as shown by the absorption spectrum. The position of the maximum (2400 A., log $\varepsilon_{max.}$ 4·31) suggests that the double bonds are situated in different rings; it is impossible to say why the position of the maximum is about 100 A. further from the visible region of the spectrum than in the dehydro-ester (VI). In addition to this diene, another compound is found in such small amount that it has not been isolated in the pure state, but from the fact that it gives an intense colour with antimony trichloride, whereas the above diene does not, it may be assumed that it is the diene (VIII) with two double bonds in one ring, analogous to amyradienol I (Picard and Spring, J., 1941, 35). This compound could be formed from norsiaresinone by reduction and loss of water :



(VIII.) (IX.)

The diene previously described (IX) is doubtless formed by a similar mechanism either from the βγ-isomeride of norsiaresinone, which might be expected to be produced to some extent by the action of alkali on norsiaresinone, or by the isomerisation of (VIII).

The stability of the ketonic acids derived from siaresinolic acid is in marked contrast to the instability of the otherwise similarly constituted acids derived from quillaic and echinocystic acids, and appears at first sight to constitute a serious objection to formula (I). Stable β-ketonic acids have, nevertheless, been observed (compare, *e.g.*, Bredt, *J. pr. Chem.*, **1937**, **148**, 221; Böttger, *Ber.*, **1937**, **70**, 316); Bredt suggests that the loss of the carboxyl group is due to a tendency on the part of the keto-group to enolise towards the carbon atom carrying the carboxyl group, and this does not take place when this carbon atom occupies a bridge head, since the structure formed would be contrary to Bredt's rule. In the case under consideration, however, it is possible for this keto-group to enolise in the opposite direction, the process being facilitated by the βγ-double bond, which tends to form a conjugated system, thus :



The system of double bonds is similar to that found in the glutaconic esters, which are also shown above. Once the enolate has been formed in the manner shown, the mechanism which normally provides the driving force for the elimination of the carboxyl group no longer operates and hydrolysis of the ester can proceed normally.

This and other reactions of siaresinolic acid cannot be satisfactorily interpreted on the basis of Haworth's original triterpene formula or the variant of it put forward by Bilham and Kon (*Nature*, **1941**, **147**, 745) (these formulæ will be found on p. 533), in which the double bond is placed in ring C, because this double bond cannot migrate to an adjacent position to become conjugated with the carbonyl group produced by the oxidation of OH[3].

Added in proof: The authors have recently obtained access to a Thesis by R. Egli (Zürich, 1933), in which some of the compounds now described are mentioned, notably methyl siaresinonate and (β) siaresinonic acid. It is remarkable that this lævorotatory acid is described as giving a dextrorotatory ester identical with methyl siaresinonate.

Experimental.

M. p.'s were determined in sealed capillaries and are uncorrected; analysis specimens were dried for 2 hours at 100°/1—2 mm.; rotations were determined in chloroform solution.

Siaresinolic Acid.—Crude sodium siaresinolate, prepared as described by Winterstein and Egli (*loc. cit.*), after being extracted with aqueous acetone (20% of water) to remove most of the colour, was suspended in water, and the acid liberated with hydrochloric acid and taken up in ether. The extract was shaken with 10% sodium hydroxide solution and the aqueous suspension of the re-formed sodium salt was separated from the ethereal layer and warmed on the steam-bath until all adhering ether had been driven off. The amorphous salt, thus rendered crystalline, was collected and washed with a little sodium hydroxide solution. The colourless salt obtained was dissolved in hot acetic acid; on cooling, the solution deposited the complex of siaresinolic acid and acetic acid, m. p. 268—270°. The yields of this product varied considerably with different samples of gum benzoin: samples A, B, and C, supplied by Messrs. Brome and Schimmer, of 6 Leather Market, S.E. 1, of moderate quality gum gave, respectively, 0·5, 0 and 0·05% of the complex; sample B contained a small amount of another triterpene (?) acid giving an ester of m. p. 244°. Specimen D, supplied by the British Drug Houses Ltd., gave a yield of 3·3% of the complex, but a specimen of equally high quality material and of exactly similar appearance, purchased from Messrs. Wright, Layman, and Umney, again contained no siaresinolic acid.

Methyl siaresinolate was prepared from the complex by treatment with diazomethane in ether and was recrystallised from methyl alcohol, forming large plates, m. p. 176°, $[\alpha]_D$ + 45° (c = 0·75). The ester (100 mg.) was recovered unchanged after boiling for 4 hours with 10 c.c. of 4% potassium hydroxide in 95% alcohol; the solution remained colourless throughout.

Methyl Acetylsiaresinolate.—500 Mg. of methyl siaresinolate were warmed with 10 c.c. of pyridine–acetic anhydride (1 : 1) until dissolved. The solution, after being left at room temperature overnight, was diluted with water, and the acetylated *ester* recrystallised from methyl alcohol, forming needles (400 mg.), m. p. 110—120°, not altered by further crystallisation (Found: C, 74·6, 74·5; H, 9·8, 9·9. $C_{33}H_{53}O_5$ requires C, 75·0; H, 9·9%).

Oxidation. The above monoacetyl ester (300 mg.) was dissolved in acetic acid (20 c.c.) and treated with a solution of 150 mg. of chromic acid in 1 c.c. of water and 5 c.c. of acetic acid. After ½ hour the solution was warmed to 60° and kept at that temperature for ½ hour; it was then cautiously diluted with hot water until crystals formed. *Methyl acetyl-21-keto-oleanolate* was then recrystallised from methyl alcohol; m. p. 232—234°; yield, 200 mg. (Found: C, 75·2; H, 9·7. $C_{33}H_{50}O_5$ requires C, 75·3; H, 9·5%).

Hydrolysis of the Acetoxy-keto-ester.—200 Mg. of the above ester were treated with 20 c.c. of 4% alcoholic potassium hydroxide, a bright yellow colour being developed at once. After 4 hours' boiling, the mixture was diluted, acidified, and extracted with ether. The acid obtained could be crystallised with some difficulty from alcohol; m. p. *ca.* 280°. It was esterified with diazomethane to the *β-hydroxy-keto-ester*, which crystallised from dilute acetone in needles, m. p. 189—190°, $[\alpha]_D$ − 195° (c = 0·935) (Found: C, 76·6, 76·6; H, 10·3, 10·3. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

Methyl α-Siaresinonate.—5 G. of methyl siaresinolate were dissolved in 200 c.c. of "AnalaR" acetic acid, and 1·5 g. of chromic acid in 50 c.c. of 90% acetic acid gradually added at room temperature. After ½ hour the mixture was kept at 60° for a further ½ hour and diluted with its own volume of hot water. Crystals gradually separated from the warm solution and were collected (3 g.); they had m. p. 207—208° and this rose to 210° on crystallisation from methyl alcohol; $[\alpha]_D$ + 135° (Found: C, 77·4; H, 9·5. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%). The *ester* was recovered unchanged after being kept for some time with sodium *iso*propoxide (warm) or sodium ethoxide (cold).

Methyl β-Siaresinonate.—500 Mg. of the above ester were boiled for 4 hours with 2 g. of potassium hydroxide in 50 c.c. of 95% alcohol. The solution at once developed a bright yellow colour. The acid, obtained by acidification and extraction with ether, crystallised from methyl alcohol in needles or prisms, m. p. 295° (decomp.), $[\alpha]_D$ − 187° (c = 0·37). On treatment with diazomethane it gave the *β-methyl* ester, which formed plates from methyl alcohol, m. p. 190° (mixed m. p. with α-ester *ca.* 165°), $[\alpha]_D$ − 192° (c = 0·79) (Found: C, 77·4; H, 9·7. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%). This ester was also prepared by the oxidation of the β-form of the hydroxy-keto-ester, obtained from the acetoxy-keto-ester, and identified by its m. p. and mixed m. p.

Reduction of α-Siaresinonic Ester.—250 Mg. of the α-ester were boiled for ½ hour with 4 g. of amalgamated zinc, 12 c.c. of acetic acid, and 2·6 c.c. of hydrochloric acid. *Methyl 21-ketodihydro-oleananate*, obtained in 40% yield by dilution and extraction with ether, crystallised from methyl alcohol in needles, m. p. 200—201°, $[\alpha]_D$ + 25·3° (c = 1·145) (Found: C 78·8, 78·6, 78·9; H, 10·5, 10·5, 10·4. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·6%). The ester showed no selective absorption of light and gave no colour with tetranitromethane. It was hydrolysed as described above; no yellow colour developed in the course of hydrolysis. The product was separated into a neutral and an acidic portion, the former of which proved to be the potassium salt of the acid. Both portions gave the same ester on warming with ethereal diazomethane, m. p. and mixed m. p. 200°, $[\alpha]_D$ + 26·7° (c = 2·285).

β-Deoxosiaresinonic Acid.—1·5 G. of methyl α-siaresinonate, 3·4 c.c. of 90% hydrazine hydrate, and 1·25 g. of sodium in 25 c.c. of alcohol were heated in a sealed tube for 12 hours at 200°. The acid obtained by acidification and extraction with ether did not crystallise. It was dissolved in ether and shaken with 10% sodium hydroxide solution, but no precipitate formed at the interface. The aqueous layer gave no precipitate on acidification, showing that the sodium salt of the acid had remained in the ethereal layer. This was therefore dried and concentrated, then diluted with light petroleum. The sodium salt separated in fine needles and could be further purified by extraction with dry ether, in which it was now sparingly soluble. The solid was dissolved in alcohol–acetic acid, giving needles of the acid, m. p. *ca.* 297° (decomp.), which were collected, washed with petroleum, and dried in a high vacuum. An attempt to reduce this acid by Clemmensen's method gave a product, m. p. 275—280° after three crystallisations from methyl alcohol, which was unaffected by diazomethane and was probably a lactone. The *methyl* ester prepared from the crude acid formed plates from methyl alcohol, m. p. 214°, $[\alpha]_D$ − 225° (c = 1·18) (Found: C, 79·2, 79·0; H, 10·2, 10·2. $C_{31}H_{48}O_4$ requires C, 79·4; H, 10·3%).

Norsiaresinone.—The above acid was heated until no more gas was evolved, care being taken to avoid charring; the product was dissolved in light petroleum (b. p. 60—80°) and percolated through a column of activated alumina, the *ketone* being adsorbed. It was eluted with benzene (yield, nearly 40%) and crystallised from acetone, giving needles, m. p. 237—238°, $[\alpha]_D$ + 152° (c = 0·80); it could also be crystallised from alcohol or light petroleum (Found: C, 84·5; H, 11·2. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3%). On one occasion a crude specimen of the acid, evidently containing some diketo-acid, was pyrolysed; after repeated crystallisation of the product from light petroleum a less soluble fraction, forming tufts of needles, m. p. 290°, was isolated; this consisted of *norsiaresinodione* (Found: C, 82·4, 82·0; H, 10·4, 10·4. $C_{29}H_{44}O_2$ requires C, 82·0; H, 10·4%).

Reduction of Norsiaresinone.—(1) The ketone was treated with hydrazine and sodium ethoxide as described on p. 543, and the product extracted with ether without previous acidification. The extract gave on evaporation a jelly, insoluble in all the solvents tried, which crystallised on digestion with methyl alcohol and acetic acid and could then be recrystallised from the latter solvent and finally from light petroleum, forming needles, m. p. 294—295°; it gave a yellow colour with tetranitromethane. The amount obtained was insufficient for analysis.

(2) 200 Mg. of norsiaresinone were reduced with zinc and acid as described on p. 543, and the product purified by percolation of its solution in light petroleum through a column of activated alumina. The solid recovered, after crystallisation from acetone and then from ethyl acetate, had m. p. and mixed m. p. with oleanene III, 218—219°, $[\alpha]_D$ + 32·1° (c = 1·93 in toluene); slow cooling of an acetone solution gave the characteristic hexagonal plates of the hydrocarbon (Found: C, 88·0; H, 11·9. Calc.: C, 87·8; H, 12·2%).

(3) 200 Mg. of the ketone in 40 c.c. of boiling absolute alcohol were gradually treated with sodium until no more would dissolve. The solution was diluted and extracted with ether, and the extract washed, dried, and evaporated. In a preliminary run it had been found that crystallisation did not give a good separation of the products formed; the residue was therefore dissolved in light petroleum (b. p. 60—80°) and percolated through a column of alumina. The first 100 c.c. of percolate contained a very small amount of solid, which could not be purified; it gave an intense colour with tetranitromethane and a deep port-wine colour with antimony trichloride in chloroform solution. The column was then eluted with benzene; the first 100 c.c. of eluate contained a solid which crystallised from methyl alcohol in flattened needles, m. p. 166—167°, consisting of *dihydronorsiaresinol*, which gave no colour with tetranitromethane (Found: C, 83·8; H, 12·1. $C_{29}H_{48}O$ requires C, 84·1; H, 12·1%).

Further elution of the column gave a solid which was unsaturated to tetranitromethane and apparently constituted a major product of the reaction. Crystallisation from methyl alcohol at first gave a product, m. p. *ca.* 180°; after crystallisation from acetic acid a product of lower m. p. was obtained, consisting of the *diene hydrocarbon*, which crystallised from methyl alcohol in plates, m. p. 126—127°, $[\alpha]_D$ − 33° (c = 0·385) (Found: C, 88·4; H, 11·8. $C_{29}H_{44}$ requires C, 88·3; H, 11·7%).

Dehydration of Methyl 2-Acetylsiaresinolate.—500 Mg. of the ester in 50 c.c. of benzene were boiled for 3 hours with 3 g. of phosphoric oxide, which assumed a deep purple colour. The colourless benzene solution was percolated through a column of activated alumina and evaporated, and the residue crystallised from methyl alcohol, giving the characteristic flattened needles of methyl acetyldehydro-oleanolate, m. p. and mixed m. p. 223—224°, $[\alpha]_D$ − 130° (c = 0·93); its absorption spectrum showed the expected maxima at 2510 A. and 2600 A. (log $\varepsilon_{max.}$ 4·45 and 4·33 respectively) (Found: C, 77·2; H, 10·0. Calc.: C, 77·5; H, 9·9%).

The authors' thanks are due to Dr. R. H. Kerlogue for the absorption spectra, and to the Royal Society for a grant.

LABORATORIES OF J. LYONS AND CO., LTD., 149 HAMMERSMITH ROAD, LONDON, W.14.
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [*Received, April 27th*, 1942.]

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105. *Sapogenins. Part XVI. The Acids of Elemi Resin.*

By PHILIP BILHAM and GEORGE A. R. KON.

A method for the separation of the two principal acid constituents of Manila elemi resin, α-elemolic and β-elemonic acid, has been developed and the properties of the pure compounds have been determined. Both acids contain two double bonds, of which only one is reactive, and they are therefore tetracyclic compounds. Measurements of unimolecular films of appropriate derivatives suggest that both acids have the carboxyl group at one end of the polycyclic system, whereas the remaining oxygen atom is situated at the opposite end of the molecule.

The double bonds of α-elemolic acid probably occupy βγ-positions with respect to each other.

MANILA elemi resin is known to contain three acids: the lævorotatory α-elemolic acid, $C_{30}H_{48}O_3$ (Tschirch and Cremer, *Arch. Pharm.*, 1902, **240**, 298; Lieb and Schwarzl, *Monatsh.*, 1924, **45**, 51), and the dextrorotatory acids, γ-elemolic, $C_{30}H_{50}O_3$, and β-elemonic, $C_{30}H_{46}O_3$ (= δ-elemic) (Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *Helv. Chim. Acta*, 1932, **15**, 681; Mladenovic, *Monatsh.*, 1932, **61**, 365). Of these, the γ-acid is not a typical constituent of the acid mixture and is only found in some samples of resin (Mladenovic, *ibid.*, 1934, **64**, 173; Lieb and Mladenovic, *ibid.*, 1931, **58**, 69); it has not been encountered in the course of the present work. The triterpene nature of α-elemolic acid follows from its dehydrogenation to sapotalene by Ruzicka *et al.* (*loc. cit.*), but although these acids are readily obtained and crystallise well, their chemistry has not been elucidated to any extent. This is no doubt due to the great difficulties attending the separation of the two principal constituents of the acid mixture: Ruzicka *et al.* (*loc. cit.*) purified the main constituent, α-elemolic acid, by means of 350 fractional crystallisations on the "triangle" principle. Lieb and Mladenovic (*Monatsh.*, 1932, **61**, 274) achieved the same end by way of the acetyl derivative and also the bromide and hydrobromide. None of these methods is suitable for the isolation of the more soluble β-elemonic acid.*

A repetition of Lieb and Mladenovic's method of purification did not give promising results, as a pure homogeneous specimen could not be obtained in spite of many wasteful crystallisations. A nearly quantitative separation is, however, possible with the aid of Girard's reagent P (Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1093) and both the α- and the β-acid can be rapidly obtained in the pure state. In this way the acid mixture yields some 70% of the α- and 10% of the β-acid, each crystallised once; the latter, especially, is obtained in a very pure condition, although from the nature of the method the principal losses fall on this compound and thus lead to an incorrect estimate of the amount originally present. This must be of the order of 15% or more; the two specimens of resin examined in the present work contained comparable proportions of the two acids.

* Since the above was written the authors' attention has been directed to an abstract of several papers by Mladenovic and his collaborators (*Chem. Abstr.*, 1940, **34**, 5451; from *Monatsh.*, 1940, **72**, 25, 35, 43), the originals of which are not available to them; in these a new method of separation of the elemi acids is described and it is concluded that α-elemolic acid has two double bonds in agreement with the present work; β-elemonic acid is stated to have three double bonds.

The properties of the pure α-acid are in good agreement with those found by Ruzicka *et al.* (*loc. cit.*), except for the appreciably higher rotation; the acetyl derivative also has the properties found by them, namely, it shrinks at 218—220° to an opaque mass which melts sharply at 232°, whereas Lieb and Mladenovic (*loc. cit.*) record the single m. p. 225°.

Pure β-elemonic acid melts lower than was found by previous investigators and its rotation is a good deal higher, namely, + 45°; it is clear that the specimens of Ruzicka, Wakeman, Furter, and Goldberg (*Helv. Chim. Acta*, 1932, **15**, 1454), $[\alpha]_D$ + 28·9°, and of Mladenovic (*Monatsh.*, 1932, **61**, 365), $[\alpha]_D$ + 32·43°, could not have been pure.

The degree of unsaturation of the elemi acids cannot be regarded as established. α-Elemolic acid is stated to have one double bond (Lieb and Mladenovic, *Monatsh.*, 1931, **58**, 59; Mladenovic, *ibid.*, 1932, **59**, 7), which is easily reduced because it forms a dihydro-derivative (Bauer, *Ber.*, 1928, **61**, 343; Lieb and Mladenovic, *loc. cit.*); Ruzicka, Hosking, and Wick (*Helv. Chim. Acta*, 1931, **14**, 811) suggest that two double bonds must be present to account for the molecular refraction of the esters and find that dihydro-α-elemolic acid gives a faint colour with tetranitromethane. β-Elemonic acid should have two reactive double bonds, because it is stated to form a tetrahydro-derivative on hydrogenation (Ruzicka, Wakeman, Furter, and Goldberg, *loc. cit.*; Mladenovic and Berkes, *Monatsh.*, 1935—6, **67**, 36), but it is now found that this is incorrect and the compound is really a dihydro-derivative. The point is one of major importance, because the number of rings in the carbon skeleton depends on the number of double bonds.

Quantitative micro-hydrogenation of both α-elemolic and β-elemonic acid reveals the presence of one reducible double bond. The reduction of the latter acid on a larger scale proceeds very rapidly and slows down distinctly as soon as two atoms of hydrogen have been introduced (compare Ruzicka *et al.*, *loc. cit.*); the *dihydro-acid* isolated at this point has the properties of the tetrahydro-compound isolated by Ruzicka *et al.*, namely, m. p. 237—238°, and forms an oxime, m. p. 236—237°. The compound prepared by Mladenovic and Berkes is stated to melt at 244°, but it has been noted throughout that the m. p.'s recorded by Mladenovic and his collaborators are several degrees higher than those found by Ruzicka and his school, or those determined in the course of the present work; there seems to be little doubt that this compound is the same as that prepared by us and it may be mentioned that the analyses recorded by Mladenovic and Berkes for the acid and the oxime all support the formula $C_{30}H_{48}O_3$ rather than $C_{30}H_{50}O_3$; the same also applies to a further analysis of the acid given by Mladenovic (*Monatsh.*, 1937, **70**, 405) and to those carried out on our specimen.

Attempts to prepare a tetrahydro-derivative by prolonging the hydrogenation for 20 hours and raising the temperature give the same acid in excellent yield and it would appear that β-elemonic acid, like the α-isomeride and α-elemolic acid, has only one double bond capable of hydrogenation. Another double bond must, however, be present, because the dihydro-acid gives a pronounced colour with tetranitromethane; it follows that β-elemonic acid must have four rings in the molecule.

Dihydro-α-elemolic acid, unlike the β-isomeride, gives only a very faint colour with tetranitromethane, so the unsaturated nature of it is not certain.* Titrations of this acid, together with the parent acid and β-elemonic acid, with permonophthalic acid in ether (Böhme, *Ber.*, 1937, **70**, 379) show that both the α- and the β-acid have one reactive double bond, which absorbs about 1·1 atoms of oxygen in 24 hours; under the same conditions, the dihydro-acid and also oleanolic acid and acetylgypsogenin methyl ester, which were used as a standard of comparison, fail to react. In an experiment of long duration (1 week), however, oleanolic acid only absorbed 0·6 atom of oxygen, and the elemi acids, about 1·3. Perbenzoic acid is known to react slowly with oleanolic acid, but the reaction is complete in a week (Winterstein and Stein, *Z. physiol. Chem.*, 1931, **202**, 222, confirmed by us); under the same conditions α-elemolic and β-elemonic acid only absorb 1·4 atoms of oxygen, and the dihydro-α-acid, 0·4 atom. The behaviour of the elemi acids thus recalls that of lanosterol derivatives (Dorée and Petrov, J., 1936, 1562; Bellamy and Dorée, J., 1941, 172, 176); it suggests that, like these, both the α- and β-acid have two double bonds and the dihydro-α-acid, one double bond. This last remaining double bond is less reactive towards perbenzoic acid than the double bond of oleanolic acid.

To obtain final confirmation of the existence of a double bond in the dihydro-α-acid, the *acetyl* derivative of its methyl ester was oxidised with selenium dioxide. This gave a *dehydro-ester*, $C_{33}H_{52}O_4$, as expected; the absorption spectrum of this compound shows a maximum at 2390 A., although the intensity is less than would be expected (log $\varepsilon_{max.}$ = 3·95). The compound was repeatedly purified by chromatographic adsorption and numerous crystallisations, but these failed to alter the properties of the compound in any way or to raise the intensity of the absorption; it must be concluded that the structure of this compound is not entirely analogous to that of the dehydro-compounds obtained by the same method from β-amyrin (Picard and Spring, J., 1941, 35; Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 767) and from methyl acetyl-oleanolate (Ruzicka, Grob, and Sluys-Veer, *ibid.*, p. 788; preceding papers), especially as the position of the absorption maximum in these compounds is at a somewhat longer wave-length, *ca.* 2500 A. The formation of our compound is, however, sufficient confirmation of the unsaturated character of the dihydro-α-acid. Further evidence of this is discussed on p. 546.

The carboxyl group of α-elemolic acid occupies a sterically protected position, because the esters are hydrolysed with difficulty, a feature observed by Ruzicka, Hosking, and Wick (*loc. cit.*) and confirmed in the present investigation. In order to gain further information as to the position of this group in the molecule, α- and β-elemolic acid and their dihydro-compounds have been converted into the oxygen-free acids.

* It has quite recently been found that acetyldihydro-α-elemolic acid gives a marked colour with tetranitromethane.

α-Elemonic acid is not reduced by the Clemmensen method or on heating with 50% hydrazine hydrate and sodium ethoxide. The methyl ester, however, is reduced with 98% hydrazine hydrate to *α-elemanic acid*, m. p. 257°, characterised by the *methyl* ester, m. p. 131—132°. Reduction of methyl α-elemonate by the Clemmensen method gives an *ester*, which crystallises with difficulty, although a portion separates in definite, palm-frond-like aggregates of needles, m. p. 87—88°. On hydrolysis these give an *iso-α-elemanic acid* which also melts at 257° and does not depress the m. p. of the acid already described, but there is a depression of the m. p. of the mixed esters. The *iso*-ester can be distinguished by the brown, not yellow, colour it gives with tetranitromethane.

Dihydro-α-elemonic acid is reduced by the hydrazine process to *dihydro-α-elemanic acid* (*methyl* ester, m. p. 99—100°) and its methyl ester is also reduced by Clemmensen's method to the same methyl ester (m. p. and mixed m. p. 98—99°).

β-Elemonic acid is reduced by the hydrazine process to a product which appears to be a mixture of two stereoisomerides: one form, A, long needles, m. p. 224—226°, is not always obtained. The other, B, forms characteristic shining spangles, m. p. 216—217°; there is no depression of the m. p. of mixtures of the acids or of their esters, both of which melt at about 115°. The acids were, indeed, regarded as two crystalline modifications of the same compound, but they form appreciably different surface films and must therefore be distinct.

Reduction of methyl β-elemonate by Clemmensen's method gives a product, which is hydrolysed to a mixture of acids; the latter is more simply obtained by the direct reduction of β-elemonic acid. After repeated crystallisation an acid, m. p. *ca.* 255°, is obtained, which was at first thought to be the *iso*-α-acid (there is no depression of the m. p. on mixing any of the elemanic acids), but the ester melted too high and was identified as *methyl dihydro-β-elemanate*. β-Elemonic acid is evidently reduced and hydrogenated at the same time on treatment with amalgamated zinc and acid, like siaresinonic ester (p. 548).

Dihydro-β-elemonic acid is reduced by the hydrazine process to *dihydro-β-elemanic acid*, m. p. 253—255° (*methyl* ester, m. p. 103—104°); it is also very readily reduced by the Clemmensen method, giving an acid melting some 5° higher than the pure dihydro-β-acid; on esterification it gives an ester consisting mainly of the dihydro-β-ester (m. p. 98—99°, depressed by addition of the α- but not the β-ester). It is difficult to decide whether the impurity in this case is the α-isomeride or some other compound. In general it may be said that pure homogeneous products are obtained by the hydrazine process and the yields are almost quantitative, whereas the Clemmensen method appears to cause a certain amount of isomerisation in every case.

The action of formic acid on (crude) α-elemolic acid has already been tried by Ruzicka, Hosking, and Wick (*loc. cit.*); it is uncertain and is accompanied by resinification, but it can be controlled by the addition of chloroform. The product, m. p. 225°, is evidently the same as theirs and gives similar figures on analysis, suggesting a *compound* of formic acid with α-elemolic acid in equimolecular proportion; it is easily hydrolysed to α-elemolic acid with alkali.

Under similar conditions β-elemonic acid gives a mixture from which a *compound*, $C_{31}H_{50}O_6$, can be isolated, corresponding to a molecule each of β-elemonic acid, formic acid, and water. It is resistant to hydrolysis and is hydrogenated to an *acid* $C_{31}H_{50}O_4$, which is still unsaturated to tetranitromethane. Although the nature of these products is uncertain, it is clear that the action of formic acid does not cause cyclisation of a tetracyclic to a pentacyclic structure.

Dihydro-β-elemonic acid and also α-elemonic acid are unaffected by boiling with formic acid.

The ready isomerisation of the unsaturated centre in the α-series is seen in the formation of esters with conjugated double bonds. α-Elemolic and α- and β-elemonic acid are optically transparent. Methyl α-elemonate, whether made from the acid or by the oxidation of methyl α-elemolate, has a distinct absorption at 2370 A. ($\log \varepsilon_{max.} = 3{\cdot}81$). This may seem remarkable, but it must be remembered that the ester, as first obtained, is not a homogeneous compound (compare Ruzicka, Hosking, and Wick, *loc. cit.*; Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*) and the m. p. gradually rises on repeated crystallisation; * it is evident that the mixture is gradually separated into the less soluble form with conjugated double bonds, which crystallises, leaving the other isomeride (or isomerides) in the mother-liquors. This may also account for the extremely tedious process of purification which is necessary to bring the m. p. of α-elemonic acid up to 274—275° even when it is prepared from purified α-elemolic acid.

The selective absorption of methyl α-elemonate is not due to the conjugation of the double bond with the carbonyl group, because it persists after the ester has been reduced either by the Clemmensen method or with hydrazine: both methyl α-elemanate and the *iso*-ester have a comparable absorption band at 2370 A. ($\log \varepsilon_{max.} = 3{\cdot}81$). None of the derivatives of the β-elemanic acids show selective absorption of light.

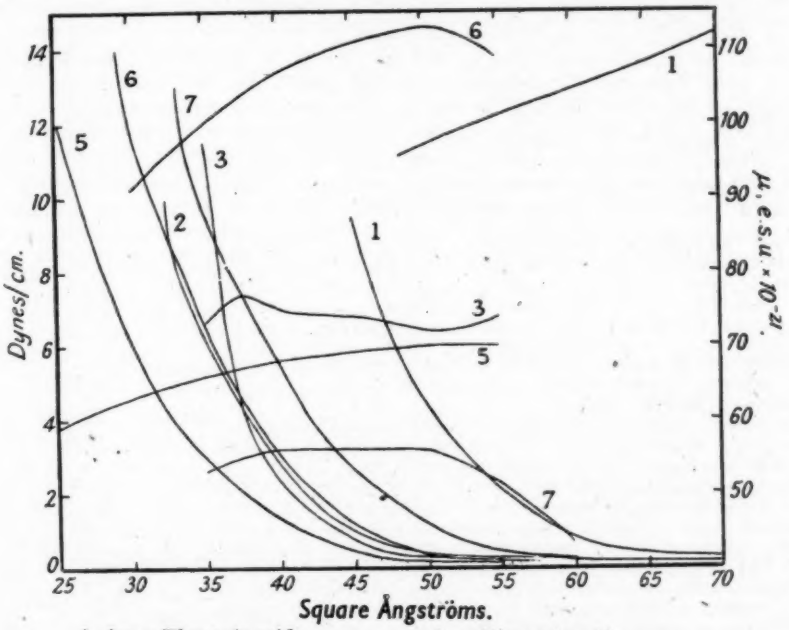
The results of surface-film measurements on the acids described above are in Table I:

TABLE I.

Compound.	Limiting area in sq. A.	μ in e.s.u. $\times 10^{-21}$.	Compound.	Limiting area in sq. A.	μ in e.s.u. $\times 10^{-21}$.
iso-α-Elemanic acid	61	89	β-Elemanic acid, B	50	113
α-Elemanic acid	52	117	Dihydro-β-elemanic acid	57·5	46
Dihydro-α-elemanic acid	49	73	Methyl α-elemonate	120	1457
β-Elemanic acid, A (needles)	45	68	Methyl β-elemonate	130	1041

* The highest m. p. observed is 166—167° or 5° higher than found by Ruzicka *et al.*

iso-α-Elemanic acid forms a solid film of medium stability which exhibits spontaneous contraction to a very marked degree. This appears to point to a molecule possessing considerable flexibility under compression and capable of rearrangement. The limiting area is comparatively large for a triterpene acid.



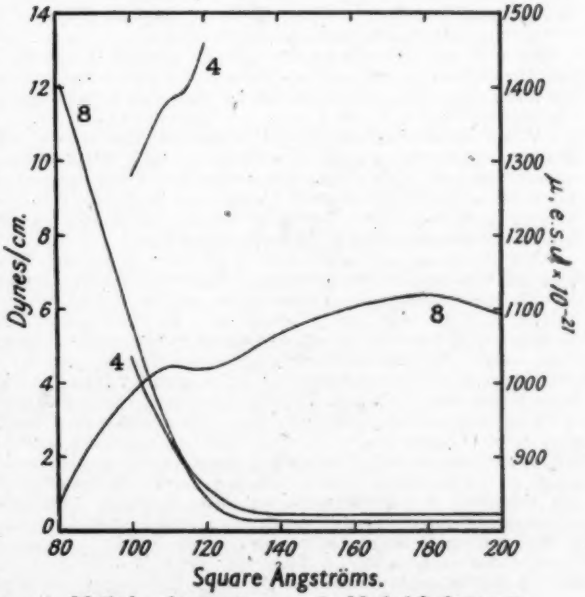
1. iso-α-*Elemanic acid.* 2. α-*Elemanic acid.*
3. *Dihydro-α-elemanic acid.* 5. β-*Elemanic acid, form A.*
6. β-*Elemanic acid, form B.* 7. *Dihydro-β-elemanic acid.*

α-Elemanic acid also exhibits marked spontaneous contraction, though to a less degree than the *iso*-acid; the limiting area is much smaller, approaching that of the dihydro-acid, whilst μ is higher. The differences between these acids could be explained on the assumption that they are the *cis*- and *trans*-forms of such a structure as (I) (below), the *cis*-form being nearer to the dihydro-acid in area.

The dihydro-α-acid exhibits spontaneous contraction to a less degree than the two diene acids, whilst the limiting area is also less, as would be expected if the double bond situated in the open-chain portion of the molecule were reduced. Films of the dihydro-acid are somewhat less compressible than those of the diene acids.

The two forms of β-elemanic acid give similar solid films, with comparable mechanical properties; those of the A form are fairly stable, with a compressibility curve similar to that of the dihydro-α-acid. On the other hand, the limiting area is lower, which is unexpected, since it suggests a more compact arrangement than is found in the more saturated compound. The B form has a somewhat larger area, but is otherwise very similar.

Dihydro-β-elemanic acid also forms similar films with marked spontaneous contraction, but the limiting area is unexpectedly large, appreciably larger than the areas of the corresponding diene acids; no reason can at present be suggested for this. The low value of μ as compared with the latter acids can be taken as some indication that the double bond which has undergone reduction in the formation of the dihydro-acid must have been situated at some distance from the carboxyl group.

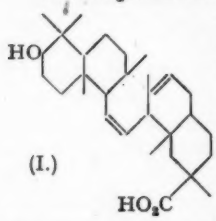


4. *Methyl α-elemonate.* 8. *Methyl β-elemonate.*

The large areas of the ketonic esters suggest that both in the α- and in the β-series of acids the carboxyl

group is widely separated from the keto-group, so that these two groups are probably situated at the opposite ends of the molecule.

The experiments described above enable us to conclude that both the α- and the β-series of elemi acids are tetracyclic compounds. Both have the carboxyl group in an end ring and the third oxygen atom is probably situated in a terminal ring at the opposite end of the molecule. The double bonds are not in sufficient proximity to the carboxyl group to form lactones, because addition products are formed with hydrogen bromide and with bromine (compare Lieb and Mladenovic, *Monatsh.*, 1931, **58**, 59); acetyldihydro-α-elemolic acid is recovered unchanged after keeping with 50% hydrobromic acid in acetic acid for 48 hours. The double bonds of the α-series are probably in the βγ-position to one another, because the optically transparent α-elemolic acid gives rise to α-elemanic esters with selective absorption; the position of the maximum at 2370 A. is in keeping with the double bonds between carbon atoms which are not heavily substituted. The available data are not sufficient to formulate these acids, but bearing in mind that they do not undergo internal cyclisation and form sapotalene on dehydrogenation, a formula such as (I) may be tentatively put forward for α-elemolic acid to serve as a basis for further discussion.



(I.)

Experimental.

M. p.'s were determined in sealed capillaries and are uncorrected. Analysis specimens were dried for 2 hours at 100°/1—2 mm. Rotations were determined in chloroform solution. The technique of surface-film measurements was that previously described (J., 1941, 552).

Separation of α-Elemolic and β-Elemonic Acids.—The crude acid mixture was obtained from elemi resin as described by Ruzicka, Hosking, and Wick (*loc. cit.*). A specimen of resin (B) supplied by Messrs. Brome and Schimmer gave a slightly smaller yield of crude acid than a sample of Merck's resin (M), but contained somewhat more of the β-acid than the latter. The acid mixture was purified by dissolving it in the minimum amount of hot acetone and gradually adding water until a slight turbidity was produced, which disappeared on warming. On cooling, the solution deposited a colourless crystalline product. Preliminary experiments with the ester prepared from this acid mixture with diazomethane showed that a separation by means of Girard's reagent was practicable, two almost equal fractions being obtained (from resin B); this was then tried with the acid itself, under the conditions described by Girard and Sandulesco (*loc. cit.*), but cutting down the amount of acetic acid used, since this was partly replaced by the elemic acid.

4·5 G. of purified mixed acids (from resin B) were boiled for ½ hour with 1·5 g. of Girard's reagent P in 30 c.c. of absolute alcohol and 2 c.c. of AnalaR acetic acid, the solution poured into 300 c.c. of ice-water containing the calculated amount of alkali to neutralise 9/10ths of the acetic acid, and the mixture extracted three times with a liberal amount of ether. Emulsions tended to form at this stage. The extract was washed with water, dried over sodium sulphate, and evaporated, and the residue of α-elemolic acid crystallised from dilute acetone. The first crop (2·45 g.) had m. p. *ca.* 218°, $[\alpha]_D$ −24·1°.

The cloudy aqueous solution obtained above was treated with 50 c.c. of concentrated hydrochloric acid, causing an immediate clearing of the solution and the separation of an ethereal layer. This was separated after a few minutes, washed, dried, and evaporated, giving a solid, which was crystallised from dilute acetone, then from dilute alcohol, and formed needles (0·45 g.), m. p. 206—209°, consisting of β-elemonic acid. Practically nothing more was extracted from the aqueous portion after several hours, showing that the hydrolysis of the compound formed by Girard's reagent with β-elemonic acid is almost instantaneous.

On a larger scale emulsions caused a good deal of trouble and it was found preferable to separate the ethereal layer and the aqueous portion as far as possible from an intermediate layer of emulsion and to let the latter stand for some time. As there was a danger of the ketonic derivative undergoing some hydrolysis, the acid from this intermediate layer was repurified.

When 100 g. of mixed acid (from resin M) were treated at once, 20 g. of Girard's reagent were used. The first ethereal extract, containing the α-acid, was washed with water and gave a very cloudy extract, which formed a stiff gel on addition of mineral acid; this cleared on addition of ether, and on extraction yielded 19 g. of crude acid consisting mainly of β-elemonic acid; 2·5 g. of pure β-acid were isolated from the ketonic fraction. The non-ketonic fraction gave a total of 70 g. of α-elemolic acid. In another experiment 95 g. of mixed acids gave 70 g. of α-elemolic and 9 g. of β-elemonic acid after retreatment of the intermediate portion.

A specimen of α-elemolic acid (from resin B) purified by two treatments with Girard's reagent (practically no ketonic fraction was isolated in the second treatment) was crystallised three times from alcohol, then from acetone, forming crystals resembling granulated sugar, m. p. 218—220°, $[\alpha]_D$ − 24·7° (c = 1·75). Another specimen (from resin M) had m. p. 218—220°, $[\alpha]_D$ − 24·5° to − 24·8° in different crystallisations, and $[\alpha]_D$ − 29° in ethyl alcohol (c = 1·595); further crystallisation caused no change in properties (Found: C, 78·8; H, 10·5; double bonds by micro-hydrogenation, 1·05. Calc.: C, 78·9; H, 10·6%; double bonds, 1 or 2).

The ester could only be obtained as a glassy resin (it was not distilled) and was recovered unchanged after refluxing for 4 hours with an excess of 20% alcoholic potassium hydroxide.

β-Elemonic acid purified by two treatments with Girard's reagent and repeated crystallisation from dilute acetone and dilute alcohol had m. p. 212—214° to a cloudy liquid clearing at 216°, $[\alpha]_D$ + 45° (c = 1·99); the specimen was recrystallised twice more without change in m. p. or rotation (Found: C, 79·2, 79·4; H, 10·4, 10·4; double bonds by micro-hydrogenation, 0·94. Calc.: C, 79·2; H, 10·2%; double bonds, 1 or 2). The acid also crystallises well from ethyl acetate or pure acetone; it forms flattened needles which separate almost completely from the warm solution, whereas the α-acid crystallises slowly and generally gives several crops of crystals, notably from alcohol. The oxime of β-elemonic acid formed needles, m. p. 212—213°.

Acetyl-α-elemolic Acid.—This was prepared in 90% yield as described by Lieb and Mladenovic (*Monatsh.*, 1931, **58**, 59); a specimen prepared from the pure acid and repeatedly crystallised had $[\alpha]_D$ − 43·5° (c = 1·36).

Acetyldihydro-α-elemolic Acid.—18·5 G. of the above acid in 400 c.c. of hot AnalaR acetic acid were added to *ca.* 200 mg. of Adams's catalyst, which had been reduced with hydrogen under 40 c.c. of the same acid. The mixture was kept warm and shaken in an atmosphere of hydrogen. After 2½ hours no further absorption appeared to take place. The liquid was filtered hot; 11 g. of the dihydro-acid crystallised from the filtrate and a further 6 g. of m. p. 242—243° were recovered by diluting the filtrate and crystallising the precipitated acid from acetone. Repeated crystallisation gave fine needles, m. p. 244—245°, $[\alpha]_D$ − 33° (c = 2·41) (Mladenovic, *Monatsh.*, 1931, **59**, 228, gives m. p. 248·5° and

$[\alpha]_D$ − 30·0°). The *methyl* ester, prepared with ethereal diazomethane, crystallised from methyl alcohol in silky needles, m. p. 135° (Found: C, 77·1; H, 10·6. $C_{32}H_{54}O_4$ requires C, 77·0; H, 10·6%).

Dihydro-α-elemolic Acid.—The hydrolysis of the acetylated acid was carried out exactly as described by Mladenovic (*loc. cit.*); the discoloration of the solution noted by him was not observed, possibly owing to the use of all-glass apparatus. The yield of acid crystallised from acetone was over 80%. The same acid was also prepared by the hydrogenation of α-elemolic acid in ethyl acetate solution, the platinum catalyst having been previously reduced under acetic acid. Some gummy material appeared to be formed in addition to the desired acid; the product was hydrolysed with potassium hydroxide to decompose any acetylated acid which might have been formed (compare Mladenovic, *loc. cit.*), but the yield of pure acid was not good. The acid repeatedly crystallised from acetone and from ethyl acetate had m. p. 230—231°, clearing at 232°, $[\alpha]_D$ − 18·7° (c = 1·415) and − 18·5° in alcohol (contrast Mladenovic, *loc. cit.*).

Methyl α-Elemonate.—α-Elemonic acid was prepared as described by Ruzicka, Hosking, and Wick (*loc. cit.*) from α-elemolic acid which had been purified by repeated crystallisation, but not by means of Girard's reagent. It was repeatedly crystallised from acetic acid, the first mother-liquors being worked up for β-elemonic acid, which was isolated in appreciable quantities (compare Mladenovic and Berkes, *loc. cit.*); the m. p. of the acid finally rose to 269—271°, but the proper m. p. 274—275° could only be attained if the substance was finally crystallised from alcohol.* The ester was prepared with diazomethane and had m. p. 158—159° after repeated crystallisation from acetone (compare Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*).

Methyl α-elemonate was also prepared by the oxidation of methyl α-elemolate, prepared by treating pure α-elemolic acid with diazomethane and distilling off the solvent. 2·5 G. of the ester were dissolved in 33 c.c. of AnalaR acetic acid, the solution cooled to 50°, and a warm solution of 900 mg. of chromic acid in 1 c.c. of water and 10 c.c. of acetic acid gradually added with shaking. After 10 minutes the mixture was diluted with water and extracted with ether, and the extract washed with alkali, dried, and evaporated. The residue solidified when rubbed with methyl alcohol and after five crystallisations from that solvent had m. p. 166—167°. Both this specimen and the one prepared from crude α-elemolic acid had an appreciable absorption of light in the region of 2370 A.

α-Elemanic Acid.—500 Mg. of methyl α-elemonate, m. p. 166—167°, were heated in a sealed tube for 16 hours at 200° with 1·3 c.c. of 98% hydrazine hydrate and 500 mg. of sodium in 10 c.c. of alcohol. The product was diluted, acidified, and extracted with ether. *α-Elemanic acid* was obtained in almost quantitative yield and had m. p. 257°, $[\alpha]_D$ − 29° (c = 1·545), after three crystallisations from alcohol, forming fine needles (Found: C, 81·3, 81·4; H, 11·0, 11·2. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). The *methyl* ester prepared with diazomethane, formed iridescent plates from methyl alcohol, m. p. 131—132° (Found: C, 81·7; H, 11·1. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·1%).

iso-*α-Elemanic Acid.*—1·9 G. of methyl α-elemonate were boiled for ½ hour with 65 c.c. of acetic acid, 15 c.c. of hydrochloric acid, and 25 g. of amalgamated zinc filings. *Methyl* iso-*α-elemanate* was isolated on dilution and extraction with ether as an oil which became opaque and semi-solid on treatment with methyl alcohol. It was purified by percolation of its solution in light petroleum (b. p. 60—80°) through a column of activated alumina and finally crystallised from methyl alcohol. It was sparingly soluble in this solvent, but separated from it slowly, forming palm-frond-like aggregates of long, brittle needles, m. p. 87°; when its solutions were rapidly cooled, it tended to separate in an amorphous condition (Found: C, 81·7; H, 11·3. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·1%). The same difficulties were encountered with this ester prepared from the pure methyl α-elemonate, m. p. 166—167°, or from the ester of m. p. 158—159°; the product appears to be a mixture of stereoisomerides.

600 Mg. of the above ester, dissolved in 60 c.c. of 20% ethyl-alcoholic potassium hydroxide, were heated in two sealed tubes for 7 hours at 180—200°. The hydrolysis was complete; the *acid* isolated by acidification and extraction with ether solidified on removal of the solvent and crystallised equally well from alcohol, ethyl acetate, or acetic acid; it was rather sparingly soluble in methyl alcohol and in acetone and comparatively sparingly soluble in chloroform. From ethyl acetate it formed aggregates of silky needles, m. p. 257°, $[\alpha]_D$ − 20° (c = 0·7) (Found: C, 81·9; H, 11·3. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%).

Dihydro-α-elemonic Acid.—α-Elemonic acid was hydrogenated in warm acetic acid solution as described on p. 548, giving a good yield of dihydro-acid, m. p. 291—292° after repeated crystallisation (compare Mladenovic, *Monatsh.*, 1932, **61**, 274). Another specimen was prepared by dropping a warm solution of 1·2 g. of chromic acid in 1 c.c. of water and 16 c.c. of AnalaR acetic acid into a mechanically stirred solution of 3·5 g. of dihydro-α-elemolic acid in 48 c.c. of acetic acid kept at *ca.* 50°. The ketonic acid began to separate from the hot solution and the separation was completed by cooling. The yield was only 1·3 g. and the mother-liquors gave on dilution a further crop of crystalline material, which was recrystallised from acetic acid. It formed prismatic crystals melting rather indefinitely at 245—255°, the m. p. being strongly depressed by admixture of dihydro-α-elemonic acid. It was at first thought to be a degradation product of the latter (Found: C, 78·1; H, 10·2%), but the *oxime* prepared from it showed that it must have been isomeric with the dihydro-acid. The oxime was prepared by boiling 200 mg. of acid with 200 mg. of hydroxylamine hydrochloride and 300 mg. of sodium acetate in the minimum amount of water and alcohol to give a clear solution. It crystallised from alcohol in needles, m. p. 234—235° (decomp.) (Found: C, 76·4; H, 10·7. $C_{30}H_{49}O_2N$ requires C, 76·4; H, 10·5%).

Methyl dihydro-α-elemonate crystallised from methyl alcohol in very fine felted needles, m. p. 172—174°; it usually melted lower than this and had a tendency to separate in a gelatinous form if the solution was too concentrated (Found: C, 79·4, 79·2; H, 10·7, 10·7. $C_{31}H_{50}O_2$ requires C, 79·1; H, 10·7%).

Dihydro-α-elemanic Acid.—400 Mg. of the above ester were heated with hydrazine hydrate and sodium ethoxide as described above. The *acid* was too sparingly soluble in methyl alcohol to crystallise well from it, but could be crystallised from ethyl alcohol, ethyl acetate, or acetic acid, forming fine needles, m. p. 277—278° (Found: C, 81·1; H, 11·0. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The methyl ester was prepared by means of diazomethane and crystallised from methyl alcohol in spangles, m. p. 99—100°; it was also prepared by reducing methyl dihydro-α-elemonate by the Clemmensen method as described above.

Reduction of Methyl β-Elemonate.—Methyl β-elemonate (Ruzicka, Eichenberger, Furter, Goldberg, and Wakeman, *loc. cit.*) had m. p. 108—109°, $[\alpha]_D$ + 30° (c = 2·405). 3 G. of this ester were reduced by Clemmensen's method as described above. The product was a colourless oil, which was purified by adsorption from its solution in light petroleum (b. p. 60—80°) by activated alumina and elution with a mixture of this solvent with benzene (1 : 1). It solidified when rubbed with methyl alcohol and formed somewhat indefinite needles after three crystallisations from this solvent, m. p. 82—83° (Found: C, 81·5; H, 11·3. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%). Attempts to improve the yield of this *ester* were unsuccessful; more drastic conditions (compare the reduction of methyl oleanonate; J., 1940, 1469) gave an uncrystallisable oil.

The ester was hydrolysed as described above; the *acid*, after numerous crystallisations from ethyl alcohol, formed felted needles, m. p. 253—255°, not depressed by *iso*-α-elemanic acid or dihydro-α-elemanic acid. An easier way of preparing the same acid is the direct reduction of β-elemonic acid by Clemmensen's method; the reduction is complete

* This also applies to the acid obtained by the oxidation of pure α-elemolic acid.

in a few minutes and the sparingly soluble product separates from the solution. After repeated crystallisation from alcohol and from ethyl acetate the acid prepared in this way formed burrs of soft needles, m. p. 258—259°, $[\alpha]_D$ + 2° (c = 0·825) (Found: C, 81·2; H, 11·2. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The acid was re-esterified; the *ester*, after repeated crystallisation from methyl alcohol, formed plates, m. p. 104—105°, not depressed by methyl dihydro-β-elemanate (Found: C, 81·5; H, 11·3. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%).

β-Elemanic Acids.—Methyl β-elemonate was reduced with hydrazine as described on p. 549. The acid, obtained in excellent yield, was crystallised from methyl alcohol; the first portion separated in characteristic hexagonal prisms adhering firmly to the walls of the containing vessel, m. p. 216—217° after repeated crystallisation, $[\alpha]_D$ + 8·7° (c = 2·405) (Found: C, 81·7; H, 11·1. $C_{30}H_{48}O_2$ requires C, 81·8; H, 11·0%). The *methyl* ester formed flattened needles from methyl alcohol, m. p. 115—116° (Found: C, 81·6; H, 10·9. $C_{31}H_{50}O_2$ requires C, 81·9; H, 11·1%). The mother-liquors from the crystallisation of this *acid B* contained another *acid*, crystallising in needles, m. p. 224—226°, $[\alpha]_D$ + 15° (c = 1·65), distinguished as the form A (Found: C, 81·7; H, 11·1%); the methyl ester formed plates, m. p. 113—114°, not depressed by the methyl ester of the acid B.

Dihydro-β-elemonic Acid.—100 Mg. of Adams's catalyst were hydrogenated under 75 c.c. of AnalaR acetic acid, 900 mg. of β-elemonic acid dropped in, and the mixture shaken in hydrogen; 54 c.c. were absorbed during 20 minutes and the absorption then slackened considerably. The *acid* was isolated by dilution and extraction with ether after removal of the catalyst, and recrystallised from ethyl acetate, the yield of product, m. p. 237—238°, being over 700 mg.; subsequent preparations gave an 80% yield of the recrystallised product. The m. p. is not changed by further crystallisation, but it is very dependent on the rate of heating and the melt does not clear until *ca.* 242°. The acid had $[\alpha]_D$ +46·7° (c = 1·285) and gave a pronounced colour with tetranitromethane (Found: C, 79·1, 79·1; H, 10·5, 10·4. $C_{30}H_{48}O_2$ requires C, 78·9; H, 10·6%). The *methyl* ester had m. p. 112—113° after crystallisation from methyl alcohol (Found: C, 78·6, 78·7; H, 10·7, 10·7. $C_{31}H_{50}O_2$ requires C, 79·1; H, 10·7%). An equally good yield of the acid was obtained by carrying out the hydrogenation exactly as described by Ruzicka, Wakeman, Furter, and Goldberg (*loc. cit.*).

Dihydro-β-elemanic Acid.—The above acid was reduced with hydrazine hydrate as described on p. 549. The *acid* obtained in almost quantitative yield was crystallised from ethyl alcohol, acetone, and finally ethyl acetate, forming fine needles, m. p. 253—254° (Found: C, 81·5; H, 11·5. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). The *methyl* ester crystallised from methyl alcohol in elongated rhombic plates, m. p. 104° (Found: C, 81·2; H, 11·5. $C_{31}H_{52}O_2$ requires C, 81·5; H, 11·5%). When the reduction of the acid was carried out by the Clemmensen method as described on p. 549, a mixture of acids was produced, which crystallised from the reaction mixture after the first few minutes. After numerous crystallisations from ethyl acetate a product, m. p. 259—260°, was obtained; the m. p. was not depressed by either of the pure dihydro-acids already described. On esterification an ester was obtained, from which on repeated crystallisation a specimen of the dihydro-β-ester was isolated, m. p. 98—99°, not depressed by the β-, but depressed by the dihydro-α-ester.

Action of Formic Acid on the Elemi Acids.—1 G. of α-elemolic acid was boiled with 10 c.c. of chloroform and 10 c.c. of absolute formic acid for an hour. Water was then added, the chloroform layer separated, and the aqueous layer extracted with ether. The combined ether–chloroform solution was washed with water, dried, and evaporated; the colourless residue solidified on scratching and crystallised from dilute alcohol in fine needles, m. p. 225° (Found: C, 73·3; H, 9·6. $C_{30}H_{48}O_3,CH_2O_2$ requires C, 74·1; H, 10·0%). 500 Mg. of this *compound* were boiled for 3 hours with 1 g. of potassium hydroxide in 15 c.c. of methyl alcohol. The acid recovered on acidification crystallised from dilute alcohol in the characteristic sparkling crystals of α-elemolic acid, m. p. and mixed m. p. 218°.

β-Elemolic acid on similar treatment with formic acid gave a mixture from which fine needles, m. p. 223—224°, were isolated on crystallisation from dilute alcohol or acetone; it showed no selective absorption of light (Found: C, 71·5, 71·8; H, 9·7, 9·7. $C_{30}H_{46}O_3,CH_2O_2,H_2O$ requires C, 71·8; H, 9·7%). When this *compound* was hydrogenated in acetic acid solution in presence of Adams's catalyst, an *acid*, needles, m. p. 237°, from methyl alcohol, was obtained; it gave a pronounced colour with tetranitromethane (Found: C, 75·7; H, 10·5. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·4%).

The authors' thanks are due to Dr. R. H. Kerlogue for the absorption spectra, and to the Royal Society for a grant.

LABORATORIES OF J. LYONS AND CO., LTD., 149 HAMMERSMITH ROAD, LONDON, W.14.
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7.

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106. *The Nature of the Carbohydrate Residue in Ovomucoid. Part II.*

By MAURICE STACEY and JOHN M. WOOLLEY.

Hydrolysis of the methylated carbohydrate residue prepared directly from ovomucoid yields *N*-acetyl 3 : 4 : 6-trimethyl glucosamine (7 mols.), *d*-mannopyranose (2 mols.), 3 : 4 : 6-trimethyl *d*-mannopyranose (1 mol.), and 2 : 3 : 4 : 6-tetramethyl *d*-galactopyranose (1 mol.). The carbohydrate residue is formulated as a hendecasaccharide having a central core of three mannose units to which are attached, by glycosidic links, seven *N*-acetyl glucosamine units and one galactose unit.

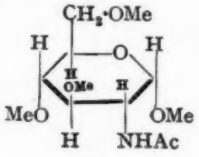
IT was mentioned in Part I (Stacey and Woolley, J., 1940, 184) that direct methylation of ovomucoid with sodium hydroxide and methyl sulphate gave the *N*-acetyl methyl derivative of the carbohydrate residue with simultaneous saponification of the peptide constituents. This direct method of methylation has been further developed, and the product shown to be homogeneous and identical with that prepared by an indirect route, namely, by the initial isolation of the carbohydrate residue, followed by its acetylation and methylation.

A suitable method for the hydrolysis of the methylated carbohydrate lay in the use of hot aqueous acid and from the hydrolysate the constituents were separated by appropriate methods. The greater part of the methylated glucosamine constituent was separated by formation of an azomethine with salicylaldehyde. 3 : 4 : 6-Trimethyl glucosamine (Cutler, Haworth, and Peat, J., 1937, 1979) condenses with salicylaldehyde to give an azomethine, from which the trimethyl glucosamine may be regenerated in 95% yield by extracting the chloroform solution of the base with 0·5N-sulphuric acid.

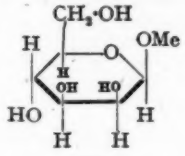
Application of this method to the aqueous hydrolysate of the methylated carbohydrate gave 3 : 4 : 6-trimethyl glucosamine hydrochloride in a yield representing 45% of the amount hydrolysed. The residual glucosamine and the mixture of hexose derivatives in the hydrolysis product were separated by methods in-

volving acetylation, glycoside formation, fractionation by solvents, and fractional distillation in a high vacuum. It was possible to follow the separation of the remaining glucosamine constituent by means of nitrogen determinations and it was identified partly as the α-form and partly as the β-form of 2-acetamido-3 : 4 : 6-trimethyl methyl-*d*-glucoside (I). Despite careful search no partially methylated glucosamine derivative was found.

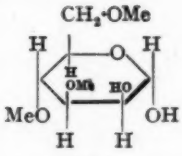
The presence of derivatives of mannose and galactose in the hydrolysis products was confirmed and these were separated and identified as α-methyl-*d*-mannopyranoside (II), 3 : 4 : 6-trimethyl *d*-mannopyranose (III), and 2 : 3 : 4 : 6-tetramethyl *d*-galactopyranoside (IV).



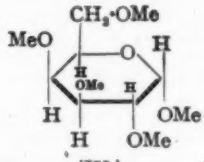
(I.)



(II.)



(III.)

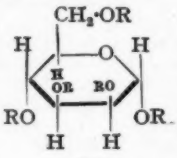


(IV.)

By a process involving the mixing and fractional distillation of corresponding fractions from a number of independent hydrolyses, it was possible to deduce an approximate quantitative estimation of the relative proportions of the constituents. These were: (i) *N*-acetyl 3 : 4 : 6-trimethyl glucosamine, 7 mols.; (ii) *d*-mannopyranose, 2 mols.; (iii) 3 : 4 : 6-trimethyl *d*-mannopyranose, 1 mol.; (iv) 2 : 3 : 4 : 6-tetramethyl *d*-galactopyranose, 1 mol. The total weight of the hydrolysis products isolated amounted to about 90% of the material hydrolysed and in view of the losses inherent in the separation this high yield is taken to indicate the probable absence of any constituent other than those described.

Discussion.

While some features of the constitution of this novel polysaccharide still remain obscure and detailed measurements of molecular size must await further investigation, it is now possible to draw certain conclusions regarding its structural pattern. It is clear from the fact that the constituent building units are glucosamine, mannose, and galactose, and from the demonstration of the high proportion of terminal units, that the carbohydrate cannot be classified as a linear polymer like starch, glycogen, or cellulose. Indeed the general structural plan more closely resembles that of the plant gums, although the latter contain uronic acid constituents and no amino-sugars. From the acetyl content (10%) of the methylated carbohydrate and from the isolation of (I) in good yield it is apparent that all the amino-groups of the glucosamine constituent are acetylated and thus do not engage in linkage with other residues. This fact, together with the identification of the whole of the glucosamine constituent as the 3 : 4 : 6-trimethyl derivative, proves that it is present in the pyranose form as terminal residues linked glycosidically to other units in the molecular complex. Since the whole of the galactose fragment was isolated as tetramethyl galactopyranose, it too must constitute a pyranose terminal residue linked glycosidically to the rest of the molecule. The attachment of all the terminal residues must in fact be to the mannose units. The existence of such a high proportion of terminal residues is compatible with the isolation of two-thirds of the mannose nucleus in the unmethylated form, the isolation of which from a fully methylated polysaccharide implies that all its hydroxyl groups are engaged in linkage to the other constituents of the saccharide in the manner shown in (V) where R is either *N*-acetylglucosamine, mannose, or galactose.



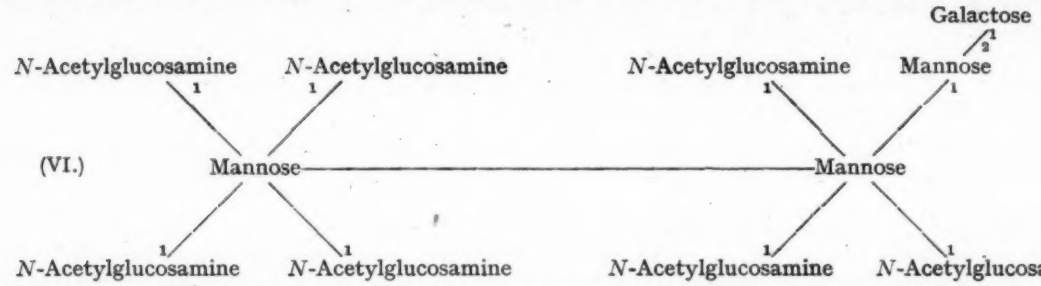
(V.)

An analogy for such an interpretation of the origin of the mannose was forthcoming from contemporaneous work in these laboratories, where *d*-xylose was shown to play a similar rôle in the structure of the β-amylase polysaccharide (Ford and Peat, J., 1941, 856) and where *l*-arabinose forms part of the structure of an araban associated with gum tragacanth (Luckett and Smith, private communication). It is likely, too, that the *l*-arabinose constituent of methylated citrus-araban (Beavan, Hirst, and Jones, J., 1939, 1865) will be shown to originate in a similar way. One-third of the mannose component in the methylated saccharide was isolated as 3 : 4 : 6-trimethyl mannopyranose and clearly is interposed between the nucleus and a terminal group, one of the linkages involved engaging C_2 of this mannose unit. Only one of the terminal units consists of galactose, but its disposition with respect to the three mannose residues has not been determined. Some support for the glycosidic mode of linkage of the *N*-acetylglucosamine constituent has recently been presented by Levene (*J. Biol. Chem.*, 1941, **140**, 279), who has isolated from a " carbohydrate-group of egg proteins " a glucosamine-mannose disaccharide in *ca.* 40% yield. The observation that reduction of this disaccharide converted the mannose moiety into mannitol led to its formulation as glucosaminido-mannose.

Based on the foregoing findings, one of several methods of portrayal of the structure of the carbohydrate residue of ovomucoid is that shown in (VI) in which, by glycosidic attachment, seven *N*-acetylglucosamine units and one galactose unit radiate from a central core of three mannose units. In this formulation the galactose unit could be interchanged with any one of the *N*-acetylglucosamine units.

The methylated derivative of such a hendecasaccharide would have N, 4·0; OMe, 34·5; *N*-acetyl, 12·0%, so that it is of interest to note that the values found for one specimen were N, 4·2; OMe, 32·0; *N*-acetyl, 10·0%. Having regard to the difficulty of assaying accurately the relative proportions of the constituents, it may well be that (VI) represents a repeating unit which in the polysaccharide is linked polymerically

through its mannose residues. Nevertheless it would appear from the nitrogen contents of the carbohydrate residue (5·5%), of its *N*-acetyl derivative (5·5%), and of its methylated derivative (4·2%), that the proportion



of glucosamine derivative (7 mols.) isolated is a minimum and that the proportion of this constituent actually present is possibly greater than that represented by 7 mols. If (VI) represented a repeating unit, it must show at least one free reducing group. This could only be the case if the maximum number of terminal glucosamine residues were six; in consequence it is considered that the above formulation, that of a hendecasaccharide, depicts the structure of the actual molecule. A number of facts support the view that the carbohydrate is not a polysaccharide in the true sense; *e.g.*, the carbohydrate itself, its acetate, and methylated derivative readily dialysed through parchment and collodion membranes; the methylated derivative showed low relative viscosities in chloroform solution, and both the acetate and the methylated derivative were easily soluble in water. Of significance, too, was the observation that the carbohydrate residue did not reduce Fehling's solution. While this molecule appears to have a structure which is unique in carbohydrate chemistry, it has been shown in these laboratories that methylated derivatives having similar physical properties can be prepared from the carbohydrates of serum mucoid, of pepsin and of gastric mucin. Indeed from the neutral carbohydrate of gastric mucin the presence of glycosidically linked glucosamine residues has been demonstrated.

In regard to the structure of the parent ovomucoid of which the carbohydrate residue forms 20%, it would seem that the peptide constituents (80%) are mainly attached to the terminal residues. Glucosamine would thus form the main connecting link between the saccharide and these peptide constituents. The fact that the latter are split off by saponification suggests that they are attached by ester linkages engaging mainly the 3-, 4-, or 6-hydroxyl groups of the amino-sugar.

Experimental.

(Unless stated otherwise, all solvents were removed by evaporation under diminished pressure.)

Direct Methylation of Ovomucoid.—The method was essentially that described in Part I (*loc. cit.*); it was found necessary, however, before completing the methylation with silver oxide and methyl iodide, to dissolve the partially methylated material in cold water and to clear the solution (centrifuge). Thereby an insoluble fraction, which did not give the Molisch test for carbohydrate and was of a lipoidal character, was separated and discarded. The average yield of methylated carbohydrate residue was 25% of the ovomucoid employed. The product had $[\alpha]_D^{20°} \pm 0°$ in water (*c*, 1·0) (Found: N, 4·2; OMe, 31·0; *N*-acetyl, 10·0%). Fractionation showed that it was essentially homogeneous, and examination of its methanolysis products confirmed its identity with material obtained by methylation of acetylated carbohydrate residue, 2-acetamido-3 : 4 : 6-trimethyl α-methylglucoside (30% yield) together with partially methylated mannose and galactose derivatives (10% yield) being isolated. Further methylation of the unidentified nitrogenous constituent with methyl iodide and silver oxide gave the light brown powder (fraction FF) described in Part I. An aqueous solution of this substance contained ionisable iodine and readily deposited silver iodide on being boiled, while negligible amounts only of crystalline derivatives could be isolated from the aqueous solution (Found: N, 2·1; AgI, 47·1. Calc. for $C_{12}H_{23}O_5NAgI$: N, 2·8; AgI, 48·1%). Its formation can be explained by the probability that methanolysis deacetylates the amino-group, which is methylated by the subsequent treatment, giving a fully methylated glucosamine; the latter then adds one molecule of silver iodide, forming a quaternary ammonium salt.

Action of Salicylaldehyde on 3 : 4 : 6-*Trimethyl Glucosamine.*—2-Acetamido-3 : 4 : 6-trimethyl β-methylglucoside (1 g.), m. p. 195°, was heated on the boiling water-bath with 2N-hydrochloric acid (50 c.c.) ($[\alpha]_D \pm 0° \longrightarrow +95°$ in 5 hours). The acid was neutralised with lead carbonate, and the filtered solution made alkaline with barium hydroxide and shaken for 6 hours with salicylaldehyde. The resulting bright yellow solution was extracted three times with chloroform, which dissolved the azomethine. Isolation of this base was unnecessary, since on shaking the chloroform solution with 0·5N-sulphuric acid it was decomposed and the 3 : 4 : 6-trimethyl glucosamine dissolved in the acid solution. The acid was removed quantitatively as barium sulphate, and the filtered solution acidified with hydrochloric acid and evaporated, giving 3 : 4 : 6-trimethyl glucosamine hydrochloride (0·82 g., 95% yield), $[\alpha]_D^{21°} +57°$ in methyl alcohol (*c*, 1·0). This method of extraction was applied, as described below, to the hydrolysis products of the methylated carbohydrate residue.

Hydrolysis of the Methylated Carbohydrate Residue with N-*Hydrochloric Acid and Isolation of* 3 : 4 : 6-*Trimethyl Glucosamine Hydrochloride.*—The methylated material (1·0 g.) was dissolved in 4% hydrochloric acid (50 c.c.), and the solution heated at 100°, $[\alpha]_D \pm 0°$; +20° (1 hour); +25° (2 hours); +28° (3 hours); +31° (4 hours); +32° (5 hours) (constant value). The solution was neutralised with lead carbonate, filtered, made faintly alkaline with barium hydroxide, and shaken for 6 hours with salicylaldehyde. The yellow solution (SY) was extracted three times with chloroform (50 c.c. portions), and the combined chloroform extracts shaken with N/10-sulphuric acid (100 c.c.). The solution was neutralised with barium carbonate, filtered, and evaporated, giving a syrup, which was dissolved in alcohol containing hydrochloric acid. Evaporation of this solution gave 3 : 4 : 6-trimethyl glucosamine hydrochloride (0·17 g.) identical with an authentic specimen. The aqueous solution (SY) was neutralised with sulphuric acid, and the filtered solution evaporated, giving a syrup fraction FY (0·31 g.). Repetition of this experiment gave an average yield of 3 : 4 : 6-trimethyl glucosamine hydrochloride (34%) and of the syrup fraction FY (65%).

Isolation of α-Methylmannoside.—The sample of methylated carbohydrate residue (8 g.) (Found: OMe, 29·1%) used in this experiment had been heated during the initial methylation stages to a higher temperature (80°) than usual.

It was treated as described above and the fraction FY (5·6 g.) (N, 2·8%) was examined. It reduced Fehling's solution, gave a positive Molisch test, and was boiled with 2% methyl-alcoholic hydrogen chloride for 5 hours; the resulting syrupy mixture of glucosides was dissolved in chloroform–ether, and dry hydrogen chloride passed in. An oily deposit, collected by filtering the solution through a cotton wool pad, was dissolved in methyl alcohol, removal of which gave a syrup, fraction FYI (2·1 g.) (N, 3·3%). The filtrate was neutralised with sodium bicarbonate, and the filtered solution evaporated, giving a second syrup, fraction FYII (3·4 g.) (N, 2·6%).

Both fractions contained glucosamine derivatives and accordingly were acetylated by boiling them with acetic anhydride (15 c.c.) and fused sodium acetate (5 g.). *O*-Acetyl groups were then removed by boiling each of the fractions with 2% methyl-alcoholic hydrogen chloride (100 c.c.) for 3 hours (Moggeridge and Neuberger, J., 1938, 748).

Products from Fraction FYI.—The non-reducing solution was neutralised with lead carbonate, filtered, and the residue washed well with ethyl alcohol. A semi-solid mass obtained on evaporation of the filtrate and washings was rubbed with a few drops of warm ethyl alcohol; light petroleum was then added to produce a cloudiness, and the solution kept for 24 hours. The crystalline product (0·70 g.) was recrystallised from absolute ethyl alcohol (Found: C, 43·3; H, 7·2; OMe, 15·1. Calc. for α-methylmannopyranoside, $C_7H_{14}O_6$: C, 43·3; H, 7·2; OMe, 16·0%), m. p. 190° alone or in admixture with authentic α-methylmannopyranoside. For confirmatory identification a portion (0·1 g.) of the crystalline material was dissolved in 2N-sulphuric acid (10 c.c.) and heated on the boiling water-bath ($[\alpha]_D$ + 77·0° ⟶ + 15·2° in 4 hours). The acid was neutralised with barium carbonate, and the filtered solution evaporated, leaving a syrup, which was dissolved in water (3 c.c.) and to which were added a few drops of phenylhydrazine acetate solution. On being kept at 20°, there was deposited the characteristic mannosephenylhydrazone, m. p. 192° alone or in admixture with an authentic specimen. The mother-liquors remaining after separation of the α-methylmannopyranoside gave 2-acetamido-3 : 4 : 6-trimethyl α-methylglucoside (1·4 g.), m. p. 148°.

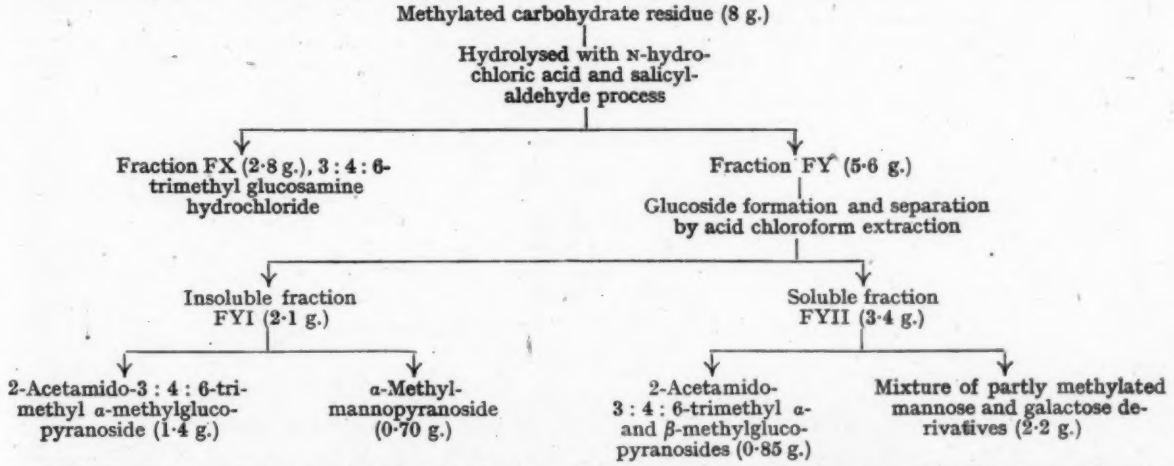
Isolation of 2-Acetamido-3 : 4 : 6-trimethyl β-Methylglucoside.—The syrupy fraction FYII was thoroughly extracted with boiling ether and from the ethereal solution a crystalline deposit (0·85 g.) was collected in four fractions: FYIIa, m. p. 195°; FYIIb, m. p. 170°; FYIIc, m. p. 172°; and FYIId, m. p. 146°. Recrystallisation of FYIIa did not change its m. p. and it was identified as 2-acetamido-3 : 4 : 6-trimethyl β-methylglucoside, $[\alpha]_D$ + 20° in chloroform (*c*, 1·1) (Found: C, 51·7; H, 8·4; N, 5·3; OMe, 44·0. Calc. for $C_{11}H_{23}O_6N$: C, 52·0; H, 8·3; N, 5·1; OMe, 44·8%).

Fraction FYIId on recrystallisation from ether had m. p. 149° alone or in admixture with 2-acetamido-3 : 4 : 6-trimethyl α-methylglucoside, and fractions YIIc and YIId were shown by fractional crystallisation methods to consist of mixtures of the α- and the β-form of 2-acetamido-3 : 4 : 6-trimethyl methylglucoside.

The part of FYII (2·2 g.) which remained insoluble in ether contained traces only of nitrogen. A portion (0·2 g.) was methylated with silver oxide and methyl iodide, and the product distilled in a high vacuum. A fraction (0·17 g.) having b. p. (bath temp.) 120—125°/0·03 mm., $n_D^{20°}$ 1·4480, was collected and dissolved in 2N-sulphuric acid (10 c.c.). On heating the solution at 100°, $[\alpha]_D^{20°}$ + 77° ⟶ + 28° (constant value) in 4 hours. The acid was neutralised with barium carbonate, and the filtered solution evaporated, leaving a syrup (0·16 g.) which was strongly reducing to Fehling's solution. The syrup was dissolved in ethyl alcohol containing a little aniline, and the solution boiled for 2 hours. Removal of the alcohol left a crystalline residue, which was extracted with boiling ether. A portion (0·08 g.) which remained undissolved in the ether had m. p. 190° alone or in admixture with 2 : 3 : 4 : 6-tetramethyl galactose anilide, and from the ethereal solution there was obtained on evaporation a substance (0·07 g.) which had m. p. 142° alone or in admixture with 2 : 3 : 4 : 6-tetramethyl mannose anilide.

Thus the previous claim (Part I, *loc. cit.*, cf. Levene, *loc. cit.*) that both mannose and galactose were constituents of the carbohydrate residue was confirmed. A search was now made in the nitrogen-free fractions of the hydrolysate for partially methylated mannose and galactose derivatives.

The fractionation procedure may be briefly summarised diagrammatically as in the table.


Methylated carbohydrate residue (8 g.)
Hydrolysed with N-hydrochloric acid and salicylaldehyde process
Fraction FX (2·8 g.), 3 : 4 : 6-trimethyl glucosamine hydrochloride
Fraction FY (5·6 g.)
Glucoside formation and separation by acid chloroform extraction
Insoluble fraction FYI (2·1 g.)
Soluble fraction FYII (3·4 g.)
2-Acetamido-3 : 4 : 6-trimethyl α-methylglucopyranoside (1·4 g.)
α-Methylmannopyranoside (0·70 g.)
2-Acetamido-3 : 4 : 6-trimethyl α- and β-methylglucopyranosides (0·85 g.)
Mixture of partly methylated mannose and galactose derivatives (2·2 g.)

Isolation of 2 : 3 : 4 : 6-Tetramethyl Methylgalactopyranoside.—Methylated carbohydrate residue (7·0 g.) was dissolved in N-hydrochloric acid, and the solution heated for 6 hours at 100°. The acid was neutralised with silver carbonate, and the filtered solution evaporated, leaving a syrup (6·5 g.), which was acetylated by being kept in contact with acetic anhydride (35 c.c.) and pyridine (70 c.c.) at 20° for 48 hours. The solvents were removed, and the syrupy product dissolved in chloroform. There remained a small amount of insoluble residue, which was removed (centrifuge) and discarded. Removal of the chloroform gave a syrup, which was boiled with 1% methyl-alcoholic hydrogen chloride. The resulting syrupy glucoside mixture (5·5 g.), isolated in the usual way, was dissolved in water (150 c.c.), and the solution warmed with charcoal, filtered, and extracted thoroughly with chloroform. The dried chloroform extract was taken down to a syrup, fraction FM (2·72 g.); the aqueous solution on evaporation also gave a syrup, fraction FN (2·70 g.). Fraction FM was exhaustively extracted with boiling ether, leaving a residue which crystallised on being rubbed with a few drops of methyl alcohol and was identified as 2-acetamido-3 : 4 : 6-trimethyl α-methylglucoside (0·90 g.). The ethereal solution gave on evaporation a syrup (1·6 g.), which was distilled in a high vacuum, giving a fraction FM_1 (0·57 g.), b. p. (bath temp.) 110—120°/0·04 mm., $n_D^{16°}$ 1·4575. The undistilled residue, fraction FM_2 (0·90 g.), was examined in the manner

described later. Fraction FM_1 (0·38 g.) was dissolved in 2N-sulphuric acid (50 c.c.), and the solution heated on the boiling water-bath; $[\alpha]_D^{20°}$ +47° (initial value); + 42° (30 mins.); + 39° (75 mins.); + 33° (120 mins.); + 27° (240 mins., constant value). The sulphuric acid was neutralised with barium carbonate, and the filtered solution evaporated, leaving a syrup (0·30 g.), which was converted into an anilide (0·1 g.) by the method previously described. When recrystallised from absolute alcohol, the anilide had m. p. 192° alone or in admixture with 2 : 3 : 4 : 6-tetramethyl galactopyranose anilide. Thus 2 : 3 : 4 : 6-tetramethyl galactopyranose was identified as being a constituent of the hydrolysis products of the methylated carbohydrate residue and it must constitute a terminal residue. In a second experiment methylated carbohydrate residue (10 g.) yielded a syrupy fraction FM_1 (0·60 g.), b. p. (bath temp.) 105—110°/0·03 mm., $n_D^{18°}$ 1·4480 (Found: OMe, 57·0. Calc. for a tetramethyl methylgalactoside: OMe, 62·0%), which was hydrolysed and converted into 2 : 3 : 4 : 6-tetramethyl galactopyranose anilide in the manner described above.

Isolation of 3 : 4 : 6-*Trimethyl Mannopyranose.*—Fraction FM_2 above (N, 0·5%) (0·80 g.) on distillation in a high vacuum gave mainly a fraction (0·65 g.), b. p. (bath temp.) 115—120°/0·03 mm., $n_D^{18°}$ 1·4592 (Found: OMe, 48·5. Calc. for a trimethyl methylhexoside, $C_{10}H_{20}O_6$: OMe, 52·0%).

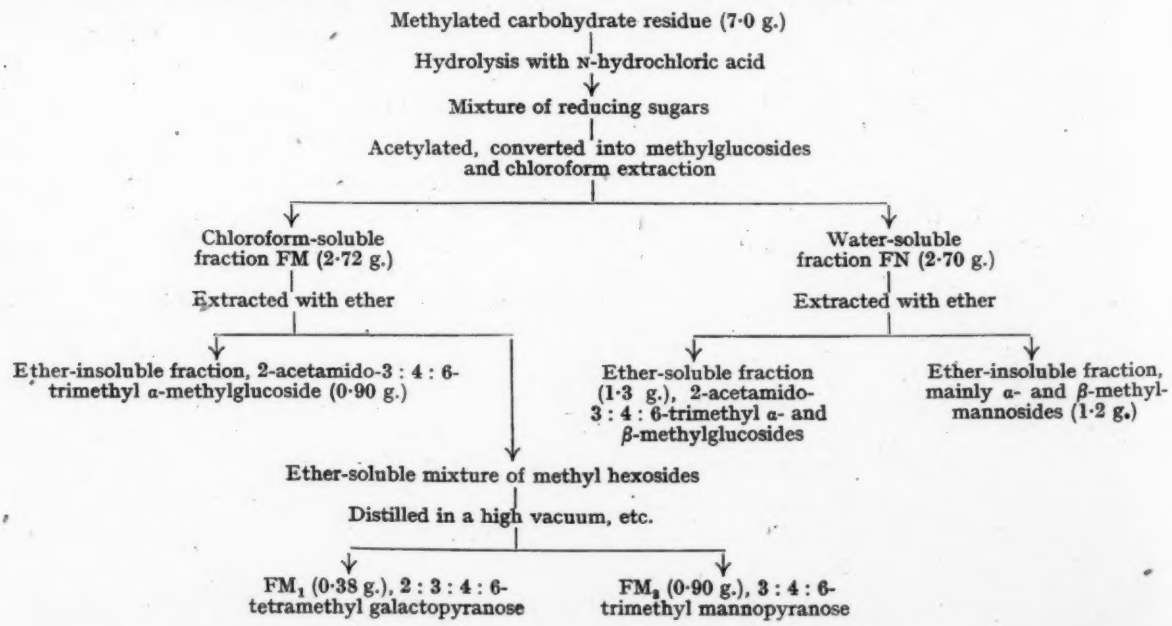
On further methylation with silver oxide and methyl iodide a portion of this syrup (0·10 g.) was converted quantitatively into 2 : 3 : 4 : 6-tetramethyl methylmannopyranoside, which was characterised by formation of 2 : 3 : 4 : 6-tetramethyl mannopyranose anilide, m. p. 142°. No tetramethyl galactose anilide was isolated in this experiment. The trimethyl methylmannoside (0·21 g.) was now hydrolysed by heating it with 2N-sulphuric acid (40 c.c.) on the boiling water-bath ($[\alpha]_D$ + 46° ⟶ + 23°, constant value, in 5 hours). The sulphuric acid was neutralised with barium carbonate, and the filtered solution taken down to a syrup, which was dissolved in ether and a small amount of inorganic material removed by filtration. Removal of the ether by slow evaporation left a crystalline mass (0·15 g.), which after recrystallisation from ether–light petroleum was identified as 3 : 4 : 6-trimethyl mannopyranose, m. p. and mixed m. p. 104°, $[\alpha]_D$ + 10°, equilibrium value in water (*c*, 1·1) (Found: OMe, 41·2. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). Careful fractionation of the mother-liquors from the separation of 2 : 3 : 4 : 6-tetramethyl galactose and 3 : 4 : 6-trimethyl mannose resulted only in the isolation of further amounts of these two compounds. No trimethyl galactose and no tetramethyl mannose fractions were identified.

Fraction FN (2·72 g.) above was thoroughly extracted with boiling ether, from which solution there was obtained a crystalline mass consisting of a mixture of 2-acetamido-3 : 4 : 6-trimethyl α- and β-methylglucosides (1·3 g.).

The syrupy ether-insoluble residue (1·2 g.) was nitrogen-free, had OMe, 14·0%, and appeared to consist mainly of a mixture of α- and β-methylmannosides which failed to crystallise. Part of this material (0·2 g.) was hydrolysed by heating it with 2N-sulphuric acid at 100° ($[\alpha]_D$ + 10°, constant value in 4 hours) and the acid was neutralised with barium carbonate. The filtered solution was strongly reducing to Fehling's solution and from it on suitable treatment with phenylhydrazine acetate small amounts of mannosephenylhydrazone and glucosephenylosazone were isolated. From the results of this and other experiments it was concluded that in order to facilitate the isolation of α-methylmannoside in crystalline form it was necessary to have recourse to methylation of the carbohydrate residue at a higher temperature than was usually employed. It appeared that at this higher temperature small amounts of protein degradation products were rendered insoluble in water, whereas at a lower temperature these substances appeared in the methylmannoside fraction and inhibited its crystallisation.

Quantitative Estimation of the Relative Amounts of the Hydrolysis Constituents.—In order to evaluate the relative proportions of the constituent units, methylated carbohydrate residue (22·5 g.) was hydrolysed and fractionated by the above methods. All unidentified fractions were then analysed for their nitrogen contents and tested for the Molisch reaction (which under the usual conditions is not given by glucosamine derivatives). Similar fractions were then combined and refractionated by solvents or distillation in a vacuum. In this way there were identified 2-acetamido-3 : 4 : 6-trimethyl *d*-glucopyranose (13·6 g.), *d*-mannopyranose (3·1 g.), 3 : 4 : 6-trimethyl *d*-mannopyranose (1·7 g.), and 2 : 3 : 4 : 6-tetramethyl *d*-galactopyranose (1·8 g.). A small amount of dark coloured material (0·5 g.) was not obtained crystalline. Allowing a 10% correction for losses during fractionation methods (Haworth and Machemer, J., 1932, 2270), it is reasonable to assume that no other derivatives are present and that the relative proportions of the constituent units of the methylated carbohydrate residue are 2-acetamido-3 : 4 : 6-trimethyl *d*-glucopyranose (7 mols.), *d*-mannopyranose (2 mols.), 3 : 4 : 6-trimethyl *d*-mannopyranose (1 mol.), and 2 : 3 : 4 : 6-tetramethyl *d*-galactopyranose (1 mol.).

The general fractionation of the hexose derivatives may be summarised briefly as follows:


Methylated carbohydrate residue (7·0 g.)
Hydrolysis with N-hydrochloric acid
Mixture of reducing sugars
Acetylated, converted into methylglucosides and chloroform extraction
Chloroform-soluble fraction FM (2·72 g.)
Water-soluble fraction FN (2·70 g.)
Extracted with ether
Extracted with ether
Ether-insoluble fraction, 2-acetamido-3 : 4 : 6-trimethyl α-methylglucoside (0·90 g.)
Ether-soluble fraction (1·3 g.), 2-acetamido-3 : 4 : 6-trimethyl α- and β-methylglucosides
Ether-insoluble fraction, mainly α- and β-methylmannosides (1·2 g.)
Ether-soluble mixture of methyl hexosides
Distilled in a high vacuum, etc.
FM1 (0·38 g.), 2 : 3 : 4 : 6-tetramethyl galactopyranose
FM2 (0·90 g.), 3 : 4 : 6-trimethyl mannopyranose

Molecular Size of the Methylated Carbohydrate Residue.—No satisfactory measurement of the molecular weight of any derivative of the carbohydrate residue has yet been obtained. Initial results from ebullioscopic methods were promising, but the work was interrupted before these could be completed. The carbohydrate residue, its acetylated, and methylated derivatives all dialysed through collodion membranes and molecular weight measurements by osmotic pressure methods were not possible. The ease of dialysis is indicative of a small molecular weight, and further evidence of this was adduced from the fact that the methylated carbohydrate residue had a very low relative viscosity in chloroform or *m*-cresol solution; in addition the acetylated and methylated derivatives were readily soluble in both cold and hot water. The carbohydrate residue did not reduce Fehling's solution.

The authors are indebted to Professor W. N. Haworth, F.R.S., for his interest and thank Messrs. Wander Bros. Ltd. for preparing the samples of dried egg-white used in the investigation.

THE A.E. HILLS LABORATORIES,
THE UNIVERSITY, EDGBASTON, BIRMINGHAM.

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107. Sophora *Alkaloids. Part IV. The Alkaloids from the Seeds of the Chatham Islands Species.*

By L. H. BRIGGS and W. E. RUSSELL.

Differences of opinion exist among botanists as to whether the *Sophora* from the Chatham Islands is a true species (*S. chathamica*) or whether it is identical with or a variety of *S. microphylla*. The alkaloids of the seeds are shown to consist of α-matrine, methylcytisine, and sophochrysine, which are all found also in the seeds of both *S. microphylla* and *S. tetraptera* but in different proportions. The chemical evidence is insufficient for a definite conclusion but tends to support the view that it is identical with *S. microphylla*.

COCKAYNE (*Trans. Roy. Soc. New Zealand*, 1902, **34**, 319), mainly in the differences exhibited by the juvenile forms, regards the *Sophora* of the Chatham Islands as a species distinct from *S. microphylla* growing on the mainland of New Zealand, which otherwise it resembles very closely, and has classified it as *S. chathamica*. Cheeseman, however ("Manual of the New Zealand Flora," 1925, p. 530), without supporting his contention, regards it as identical with or at the most a variety of *S. microphylla*. It was considered that a chemical investigation of the seeds of this *Sophora* for alkaloids would aid the botanical classification. Manske (*Canadian J. Res.*, 1939, **17**, *B*, 1) has already shown that species of *Senecio*, taxonomically indistinguishable, can be separated quite easily by the fact that they contain different alkaloids, and Baker and Smith ("A Research on the Eucalypts and their Essential Oils," 1920, Second Edition) have also demonstrated that eucalypt species, taxonomically indistinguishable, can be separated by differences in the constituents of their essential oils.

A small quantity of seeds of the *Sophora* species from the Chatham Islands has been examined for alkaloids by methods similar to those described in Parts I and II (J., 1937, 1795; 1938, 1206) for *S. microphylla* and *S. tetraptera* respectively. From the distilled bases (yield, 1·5%), three alkaloids have been identified, *viz.*, α-matrine, methylcytisine, and sophochrysine (cf. Part III, this vol., p. 507).

The same three bases also occur in *S. microphylla* and *S. tetraptera*, the main alkaloids being α-matrine and methylcytisine in both cases but in different proportion. The seeds of the former also contain cytisine and a fifth base (Base E) but these are only present to a very small extent (6 mg. and 3 mg. respectively were isolated from a much larger quantity of alkaloidal material) and would not be expected to be isolated in this case. With the small amount of material available from the Chatham Islands *Sophora* it has been impossible to separate the mixtures of bases in any way quantitatively and consequently a definite conclusion cannot be reached regarding the chemical evidence supporting the classification. The fact, however, that the alkaloids are the same as those of *S. microphylla*, together with the evidence of Manske's observations, would tend to support Cheeseman's view that the two species are identical.

The definite identification of sophochrysine from this *Sophora* supports our opinion (cf. Part III) that the base D of *S. microphylla* is identical with sophochrysine.

EXPERIMENTAL.

515 G. of the seeds of the Chatham Islands *Sophora* were worked up as described in Part II, trichloroethylene completely removing the alkaloids from the aqueous solution in 192 hours. The crude alkaloids on distillation afforded two fractions, (*a*) b. p. 180—185°/0·5 mm., (*b*) b. p. indefinite/0·8 mm. (bath temp. 260—340°)—total yield, 3·31 g. (1·5% based on weight of dry seeds).

Both fractions dissolved almost completely in hot light petroleum (b. p. 80—100°), leaving an amorphous residue (4 mg.) of base C, m. p. 284—288°. As no crystalline material had separated from the light petroleum solution after some months, the solvent was removed, and the residue digested successively with light petroleum (b. p. below 40°) and (b. p 80—100°). After concentration of the former extract colourless needles separated, m. p. 56—64°, raised by repeated crystallisation from the same solvent to 73—77° (base A). The latter extract on concentration gave colourless needles of base B, m. p. 128—132°. The yield in both cases was less than 50 mg.

Base A.—This base, m. p. 73—77°, has been identified with α-matrine, an authentic specimen causing no depression of the m. p. The picrate, crystallised from hot water, had m. p. 58—145°. The same indefinite m. p. is recorded in Part II. The aurichloride from the base (10 mg.) crystallised from the reaction mixture in golden-yellow needles, m. p. 197—199° with sintering at 195°, undepressed by an authentic specimen.

The following two new salts were prepared from matrine *ex S. tetraptera*: The perchlorate separated as an oil on addition of 20% aqueous perchloric acid to a solution of the base in ethyl acetate, but crystallised from absolute alcohol–

chloroform in colourless needles, m. p. 214·5—216°. The hydrobromide, prepared in absolute alcohol, crystallised from absolute alcohol–ethyl acetate in colourless needles, m. p. 272—275° with sintering at 266°.

Base B.—This base, m. p. 128—132°, has been identified as methylcytisine by its m. p., and by preparation of the following derivatives; in all cases the m. p.'s were not depressed by authentic specimens. The picrate crystallised from hot water in long yellow needles, m. p. 223—225° with sintering at 212° (lit., m. p. 229°; cf. Part I). The picrolonate crystallised from dilute alcohol in needles, m. p. 218° (decomp.) (Part II records 224—225°).

Base C.—This base, m. p. 284—288°, has been identified as sophochrysine by its m. p. The aurichloride prepared from it (4 mg.) crystallised in yellow needles, m. p. 187—189°. In each case the m. p. was undepressed by an authentic specimen.

We are indebted to Mr. G. G. Briggs, LL.B., Hamilton, for the collection of the seeds from the Chatham Islands and to the Chemical Society for a grant.

AUCKLAND UNIVERSITY COLLEGE, AUCKLAND, NEW ZEALAND. [*Received, May 15th*, 1942.]

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108. *Alkyl–Oxygen Fission in Carboxylic Esters. Part I. Esters of αγ-Dimethylallyl Alcohol and other Substituted Allyl Alcohols.*

By MICHAEL P. BALFE, HENRY W. J. HILLS, JOSEPH KENYON, HENRY PHILLIPS, and BERTIE C. PLATT.

Reactions of the optically active hydrogen phthalate and benzoate of αγ-dimethylallyl alcohol with acids and with alcohols, are described in which the products (esters and ethers) are extensively racemised. When the reaction is stopped before it reaches completion, the unreacted ester recovered is in many cases found to have undergone some racemisation.

Recorded instances of similar reactions of esters of other substituted allyl alcohols are quoted; in some of these, besides racemisation, rearrangement occurs in the substituted allyl residue. The rearrangement and racemisation are evidence that fission of the reacting molecule occurs at the bond joining the substituted allyl residue to the oxygen atom of the acid residue. This mechanism is in contrast to the usual mode of reaction of esters (particularly of saturated aliphatic alcohols), in which this bond remains undisturbed.

THE convenient terms alkyl–oxygen fission and acyl–oxygen fission were introduced by Day and Ingold (*Trans. Faraday Soc.*, 1941, **37**, 686) to refer to the two alternative modes of fission, (I) and (II), which may be involved in reactions of carboxylic esters:

R′·CO·O↓R″ (I) Alkyl–oxygen fission. R′·CO·↓OR″ (II) Acyl–oxygen fission.

Mechanism (II) is generally accepted as the common mode of reaction of esters, but mechanism (I) occurs, more commonly than has been realised, when the alkyl group R″ has electron-releasing properties. To the types of esters found to undergo alkyl–oxygen fission (see preliminary note, Balfe and Kenyon, *Nature*, 1941, **148**, 196), may be added the esters of *tert.*-butyl alcohol, which react with methyl alcohol to give methyl *tert.*-butyl ether (Cohen and Schneider, *J. Amer. Chem. Soc.*, 1941, **63**, 3383). When the alkyl group R″ separates as a kation, the occurrence of alkyl–oxygen fission may be demonstrated in two ways: if the carbon atom which in R″ is attached to oxygen is asymmetric, much racemisation will occur, and if the group R″ is unsaturated in the position βγ to the carbon atom which is attached to oxygen, rearrangement occurs. In acyl–oxygen fission, racemisation or rearrangement is not possible.

At an early stage in our investigations on the α- and γ-substituted allyl alcohols, the occurrence of alkyl–oxygen fission was indicated by the racemisation occurring during saponification of the hydrogen phthalates of the optically active alcohols by dilute aqueous alkali. Kenyon, Partridge, and Phillips (J., 1936, 85), in the case of γ-phenyl-α-methylallyl alcohol, indicated that a mechanism of type (I) was involved. Other recorded instances are the saponification of the hydrogen phthalates of αγ-dimethylallyl alcohol (Hills, Kenyon, and Phillips, J., 1936, 576) and of γ-methyl-α-ethylallyl alcohol (Airs, Balfe, and Kenyon, this vol., p. 18). The topic was discussed by Arcus and Kenyon (J., 1938, 1912), but no further instances have been recorded, because in experiments with other substituted allyl alcohols concentrated (5N) aqueous or aqueous-alcoholic sodium hydroxide was used for the saponification in order to obtain the alcohols with complete retention of optical purity, by the acyl–oxygen fission mechanism. Rearrangement, also, has been observed in the alkyl–oxygen fission reaction. Under weakly alkaline conditions of saponification, the hydrogen phthalate of α-phenyl-γ-methylallyl alcohol yields γ-phenyl-α-methylallyl alcohol (Kenyon, Partridge, and Phillips, J., 1937, 207).

We now describe solvolytic reactions of the optically active hydrogen phthalates and benzoates of αγ-dimethylallyl alcohol with acids and alcohols, and refer to cases of similar reactions of esters of other substituted allyl alcohols. The results obtained with the αγ-dimethylallyl compounds are summarised in the table. We are unable to attach any importance to the relative configurations of the optically active fractions of the products, since these are insignificant in amount, compared with the racemic fractions. Rearrangement in the reactions of αγ-dimethylallyl derivatives cannot be observed on account of the symmetrical substitution in the allyl residue.

These reactions have two characteristic features: (i) the extensive racemisation of the product; (ii) the racemisation found in the recovered portion of the reacting ester, when the reaction is stopped before it has reached completion. Both features indicate alkyl–oxygen fission, and the fact that the esters racemise more quickly than they react is in agreement with the known unimolecular mechanism of solvolytic reactions. The

reacting ester ionises, a process which involves solvation, and the liberated and racemised carbonium kation may recombine with the anion, or combine with a solvent molecule, from which it expels a proton. The present experiments do not exclude the possibility that the reaction product undergoes continued racemisation by solvolysis, and our view of the mechanism of the reaction may be illustrated as follows :

$$R'\cdot CO\cdot OR'' \rightleftharpoons \overset{\oplus}{R}'' + R'\cdot C\overset{\ominus}{O}\cdot O$$
$$\Big\downarrow R'''OH$$
$$R''OR''' + H^{\oplus}$$

At 66° the hydrogen phthalate of αγ-dimethylallyl alcohol reacts with methyl alcohol, giving a methyl ether of very low rotatory power, and if part of the phthalate is recovered, it is found to be extensively racemised. At 31°, in methyl alcohol, neither reaction nor racemisation occurs, a solution of the phthalate remaining unchanged in rotatory power during 3 months, but in nitromethane, the phthalate undergoes much racemisation and some decomposition during 2 months : presumably the higher dielectric constant of nitromethane facilitates ionisation of the ester, and hence racemisation and decomposition.

Reactions involving alkyl–oxygen fission have been recorded for the following hydrogen phthalates (those marked with an asterisk have been shown to involve rearrangement as well as racemisation): γ-phenyl-α-methylallyl with methyl alcohol, and α-phenyl-γ-methylallyl with methyl alcohol * and with acetic acid * (Kenyon, Partridge, and Phillips, *loc. cit.*); propenylallylcarbinyl with formic acid (Duveen and Kenyon, *Bull. Soc. chim.*, 1938, **6**, 704); γ-methyl-α-propylallyl with formic acid and with benzoic acid (Arcus and Kenyon, *loc. cit.*); α-phenylallyl with methyl and ethyl alcohols, and with formic * and acetic * acids (Duveen and Kenyon, J., 1939, 1697); γ-methyl-α-ethylallyl with methyl alcohol (Airs, Balfe, and Kenyon, *loc. cit.*).

During acid-catalysed etherification of αγ-dimethylallyl alcohol, much racemisation occurs also (three examples are recorded in the table). In etherification one or other of the reacting molecules must undergo alkyl–oxygen fission, and in the present cases this presumably occurs more readily in the unsaturated than in the saturated alcohol (methyl or *n*-butyl) with which it is reacting. The possibility that the ether itself is racemised in the presence of acid is not excluded by the present experiments.

In some of our early experiments we examined the reaction of hydrogen phthalates of optically active alcohols with sodium acetate in acetic acid solution, the products in all cases being racemic acetates. We discontinued these experiments because in this type of reaction there may be, not only alkyl–oxygen fission (interchange of anions) resulting in either racemisation or inversion of configuration, but also acyl–oxygen fission, as pointed out by Arcus, Balfe, and Kenyon (J., 1938, 485) with reference to the analogous case of sodium formate in formic acid solution, which results in retention of configuration. It is therefore not possible to draw any conclusion from the stereochemical nature of the products, which may be formed by concurrence of the two possible modes of reaction. This objection does not apply to the use of such mixtures in reactions with halides which can only react by replacement mechanisms analogous to the alkyl–oxygen fission of esters.

Reactions of the Optically Active αγ-Dimethylallyl Alcohols and their Esters.

Reacting ester of αγ-dimethylallyl alcohol.	Reactant.	Temp.	Duration.	Resulting cmpd. of dimethylallyl alcohol.	% Optical purity of resulting cmpd.	% Optical purity of recovered portion of reacting ester.
Hydrogen phthalate	$H\cdot CO_2H$ ‡	20°	5 mins.	Formate	0	0
		20	15 ,,	,,	1 †	93
		90	30 ,,	,,	0	11
	$Me\cdot CO_2H$	37	60 days	Acetate	1 †	23
		90	3½ hrs.	,,	0	0
	MeOH	64	21 hrs.	Methyl ether	6	6
		31	3 months	No reaction	—	100
	n-BuOH	90	30 hrs.	*n*-Butyl ether	9 †	19
	$Ph\cdot CH_2\cdot OH$	90	10 hrs.	Benzyl ether	2 †	8
	Ph·OH §	20	14 days	*Phenyl ether*	low	53
		90	1 hr.	,,	0	0
Benzoate	$H\cdot CO_2H$	90	6 hrs.	Formate	0	30
	$Me\cdot CO_2H$	90	50 ,,	Acetate	4 *	—
	MeOH	31	7 days	Methyl ether	4 †	98
		64	2½ ,,	,,	0	—
	n-BuOH	90	2½ ,,	*n*-Butyl ether	12 †	58
Acid catalysed reactions of (−)αγ-dimethylallyl alcohol	Dimethylallyl alcohol	20	12 hrs.	*Dimethylallyl ether*	18 *‖	—
	MeOH	20	24 ,,	Methyl ether	2 ¶	—
	n-BuOH	20	18 ,,	*n*-Butyl ether	0 ¶	—

* Retention of configuration.
† Inversion of configuration.
‡ In the first experiment a higher proportion of formic acid was used than in the second, and the proportion of formic acid used in the third was the lowest in the three.
§ In the experiment at 20°, the molar ratio of phenol to hydrogen phthalate was 3 : 1, and at 90° it was 1 : 1.
‖ % of maximum known rotation of the ether, which may not be optically pure.
¶ Hills, Kenyon, and Phillips (*loc. cit.*).

Experimental.

The preparation and rotatory powers of (+)$\alpha\gamma$-dimethylallyl alcohol and its formate, acetate, and methyl, *n*-butyl, and benzyl ethers are recorded by Hills, Kenyon, and Phillips (*loc. cit.*). In the following experiments, the reacting esters had the rotatory powers of the optically pure substances, unless otherwise stated: (+) and (−) are used to refer to optically pure dextro- and lævo-rotatory substances, respectively.

Reactions of the Optically Active $\alpha\gamma$-Dimethylallyl Hydrogen Phthalates.—(i) *With formic acid.* (*a*) At 20°. The (+)hydrogen phthalate (1 g.) dissolved instantly in formic acid (20 c.c.) with separation of phthalic acid. Within 5 mins. the filtered solution was found to be optically inactive. In the second experiment, the (+)phthalate (13 g.) was triturated with 20 g. of formic acid for 15 mins. Anhydrous ether (40 c.c.) was added, and phthalic acid (2·7 g.) filtered off. The filtrate was extracted with aqueous sodium carbonate, from which, after acidification, 8·6 g. of (+)$\alpha\gamma$-dimethylallyl hydrogen phthalate were recovered with $[\alpha]_{5893}$ + 22·1°, $[\alpha]_{5461}$ + 28·0° in chloroform (*l*, 2; *c*, 5·24). From the ethereal residue, $\alpha\gamma$-dimethylallyl formate was obtained, b. p. 122—123°, $n_D^{20°}$ 1·4125; $\alpha_{5461}^{18°}$ + 0·23° (*l*, 0·5).

(*b*) At 90°. The hydrogen phthalate (11·7 g.; $[\alpha]_{5461}$ − 26·0° in chloroform) and formic acid (2·5 g.) were warmed on the steam-bath for 30 mins. By the method described above, the following products were then isolated: phthalic anhydride (0·5 g.), $\alpha\gamma$-dimethylallyl hydrogen phthalate (4·0 g., $[\alpha]_{5461}$ − 3·4° in chloroform), *dl*-dimethylallyl formate.

(ii) *With acetic acid.* (*a*) At 37°. A solution of 20 g. of the (+)hydrogen phthalate in 75 g. of glacial acetic acid was kept at 37° for 2 months, and the following products were then isolated by the method described above: $\alpha\gamma$-dimethylallyl hydrogen phthalate (7 g., $[\alpha]_{5893}$ + 6·4°; $[\alpha]_{5461}$ + 7·0° in chloroform), $\alpha\gamma$-dimethylallyl acetate (5 c.c., b. p. 41°/11 mm., $\alpha_{5893}^{17°}$ + 0·23°, $\alpha_{5461}^{17°}$ + 0·27°, $\alpha_{4358}^{17°}$ + 0·50°, *l*, 0·5).

(*b*) At 90°. The hydrogen phthalate (5·8 g., $[\alpha]_{5461}$ − 13·4° in chloroform) and glacial acetic acid (1·7 c.c.) were heated on the steam-bath for 3½ hrs. The following products were then isolated as described above: phthalic acid (1·5 g.), *dl*-$\alpha\gamma$-dimethylallyl hydrogen phthalate (2·1 g.), *dl*-$\alpha\gamma$-dimethylallyl acetate, b. p. 137—138°. Phthalic anhydride (0·25 g.) was separated by filtration, being insoluble both in aqueous sodium carbonate and in ether.

(iii) *With methyl alcohol.* A solution of the (+)hydrogen phthalate (19 g.) in dry methyl alcohol (90 c.c.) was heated under reflux for 21 hrs., then concentrated. Addition of three successive portions of methyl alcohol (15 c.c.) to the solid residue, each followed by reconcentration, removed all volatile material. The solid residue was extracted with chloroform, from which $\alpha\gamma$-dimethylallyl hydrogen phthalate (0·5 g., $[\alpha]_{5461}$ + 1·8° in chloroform) was isolated. Phthalic acid (9·3 g.) remained undissolved. The volatile fraction was diluted with dry ether (300 c.c.), and powdered anhydrous calcium chloride (160 g.) added to remove methyl alcohol. After 12 hrs. the solid was removed by filtration and washed with ether. On concentration of the filtrate, methyl $\alpha\gamma$-dimethylallyl ether (4·0 c.c.) was obtained, b. p. 90—91°. It was redistilled until refractive index and rotatory power were constant, and then had $n_{5893}^{17°}$ 1·4038; $\alpha_{5461}^{18°}$ + 0·81°; $\alpha_{4358}^{18°}$ 1·42° (*l*, 0·25) (Found: C, 71·1; H, 11·4. Calc. for $C_6H_{12}O$: C, 72·0; H, 12·0%).

(iv) *With* n-*butyl alcohol.* A solution of the (+)hydrogen phthalate (20 g.) in *n*-butyl alcohol (60 c.c.) was heated on the steam-bath for 30 hrs., then diluted with ether and washed with dilute aqueous sodium carbonate from which, on acidification, $\alpha\gamma$-dimethylallyl hydrogen phthalate (10·8 g.) was obtained with $[\alpha]_{5461}$ + 5·83° in chloroform. The ethereal solution was then washed with water, dried, and distilled. The fraction, b. p. 150—151°, was redistilled, yielding *n*-butyl $\alpha\gamma$-dimethylallyl ether, b. p. 151—152°, $n_{5893}^{19°}$ 1·4175; $d_{4°}^{25°}$ 0·7880; $\alpha_{5461}^{20°}$ + 0·68°; $\alpha_{4358}^{20°}$ + 1·10° (*l*, 0·25) (Found: C, 75·8; H, 12·0. Calc. for $C_9H_{18}O$: C, 76·1; H, 12·7%).

(v) *With benzyl alcohol.* A solution of the hydrogen phthalate (11·7 g.; $[\alpha]_{5461}$ − 26·0° in chloroform) in benzyl alcohol (7 g.) was heated on the steam-bath for 10 hrs., then cooled, and treated as in (iv), $\alpha\gamma$-dimethylallyl hydrogen phthalate (3·2 g.) being recovered with $[\alpha]_{5461}$ − 2·0° in chloroform. The ethereal solution was washed with water, dried and distilled. The less volatile fraction was heated for 8 hrs. on the steam-bath with phthalic anhydride (8 g.) to remove benzyl alcohol, then diluted and washed as in (iv), and washed with water, dried, and distilled. Benzyl $\alpha\gamma$-dimethylallyl ether (3·3 c.c.) was obtained, b. p. 117—119°/20 mm.; $n_{5893}^{16°}$ 1·4994; $\alpha_{5461}^{20°}$ − 0·16° (*l*, 0·25) (Found: C, 81·4; H, 9·1. Calc. for $C_{12}H_{16}O$: C, 81·8; H, 9·1%).

(vi) *With phenol.* (*a*) At 20°. A solution of the (+)hydrogen phthalate (23·4 g., 1 mol.) and phenol (29 g., 3 mols.) in dry ether (50 c.c.) after 14 days at room temperature (during which phthalic acid separated) was made alkaline and extracted with ether. From the extract, *phenyl $\alpha\gamma$-dimethylallyl ether* (3 c.c.) was obtained, b. p. 97°/13 mm.; $n_{5893}^{20°}$ 1·5090; α_{5893} − 0·32°; α_{5461} − 0·34°; α_{4358} − 0·55° (*l*, 0·5) (Found: C, 81·7; H, 8·6. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%). From the aqueous residue, by acidification, $\alpha\gamma$-dimethylallyl hydrogen phthalate (15 g.) was obtained, $[\alpha]_{5461}$ + 16·0° (*c*, 5·05) in chloroform.

(*b*) At 90°. The hydrogen phthalate (11·7 g., 1 mol.; $[\alpha]_{5461}$ − 26·0° in chloroform) and phenol (5·2 g., 1 mol.) were heated together on the steam-bath for one hour, then diluted with ether, filtered from deposited phthalic acid (6 g.), washed with dilute aqueous sodium carbonate (from which *dl*-$\alpha\gamma$-dimethylallyl hydrogen phthalate was recovered), dried, and fractionally distilled; *dl*-phenyl $\alpha\gamma$-dimethylallyl ether (1·3 c.c.) was obtained, b. p. 121—122°/22 mm., $n_{5893}^{19°}$ 1·5107 (Found: C, 81·7; H, 8·6%).

The relative configuration and rotatory power of optically pure phenyl $\alpha\gamma$-dimethylallyl ether could not be determined, as it was not possible to prepare it from the carbinol by methods unlikely to cause configurational change.

Reactions of $\alpha\gamma$-Dimethylallyl Benzoate.—(i) *With formic acid.* The (+)benzoate (7 g.) and anhydrous formic acid (2 c.c.) were heated on the steam-bath for 6 hrs., cooled, diluted with ether, washed with dilute aqueous sodium carbonate and, after removal of the ether, fractionally distilled. From the more volatile fraction, on redistillation, *dl*-$\alpha\gamma$-dimethylallyl formate (2 c.c.) was obtained, b. p. 122—123°; $n_{5893}^{15°}$ 1·4163; $\alpha_{5461}^{20°}$ − 0·22° (*l*, 0·5). The less volatile fraction yielded $\alpha\gamma$-dimethylallyl benzoate (2·5 c.c.), b. p. 132—134°/19 mm.; α_{5461} + 1·94°; α_{4358} + 3·9° (*l*, 0·25). From 20·9 g. of the benzoate ($\alpha_{5461}^{20°}$ − 4·46°; *l*, 0·25) and 5·4 g. of formic acid, heated on the steam-bath for 20 hrs., 3 c.c. of *dl*-formate were obtained (Found: C, 63·3; H, 8·8. Calc. for $C_6H_{10}O_2$: C, 63·1; H, 8·8%).

(ii) *With acetic acid.* The benzoate (21·4 g.; $\alpha_{5461}^{20°}$ − 7·56°, *l*, 0·5) and glacial acetic acid (7·3 c.c.) were heated together on the steam-bath for 50 hrs., then fractionally distilled. The more volatile fraction, dried and redistilled, yielded $\alpha\gamma$-dimethylallyl acetate (2 c.c.), b. p. 136—137°; $n_{5893}^{15°}$ 1·4218, $\alpha_{5461}^{20°}$ + 0·36° (*l*, 0·25).

(iii) *With methyl alcohol.* (*a*) At 31°. A solution of the benzoate (19 g.; $\alpha_{5461}^{18°}$ + 11·3°, *l*, 0·5) in 40 g. of dry methyl alcohol, after standing at 31° for 7 days, was distilled on the steam-bath, 20 g. of methyl alcohol being added in portions towards the end of distillation to facilitate removal of the methyl ether. The combined distillates were placed on powdered anhydrous calcium chloride overnight, and the resulting pasty mass lixiviated with dry ether. The ethereal extract was concentrated and the residue distilled, yielding: (i) methyl $\alpha\gamma$-dimethylallyl ether (4 c.c.), b. p. 90°, $n_{5893}^{18°}$ 1·4046, $\alpha_{5461}^{19°}$ + 1·02°, $\alpha_{4358}^{19°}$ + 2·0° (*l*, 0·5); (ii) methyl benzoate (6 g.), b. p. 199—200°, $n_{5893}^{20°}$ 1·5148 (Perkin, J., 1896, **69**, 1174, gives b. p. 199°; Cotton and Moulton, *Ann. Chim. Phys.*, 1913, **28**, 214, give $n_{5893}^{18·7°}$ 1·5144); (iii) recovered $\alpha\gamma$-dimethylallyl benzoate, b. p. 125—126°/14 mm., $\alpha_{5461}^{18°}$ + 11·1° (*l*, 0·5); (iv) benzoic acid (4·7 g.).

(*b*) At 64°. The benzoate (6·3 g.; $\alpha_{5461}^{20°}$ − 6·7°, *l*, 0·5) in methyl alcohol (50 c.c.) was heated under reflux for 60 hrs., then treated as in (*a*). *dl*-Methyl $\alpha\gamma$-dimethylallyl ether (2 c.c.) was obtained, b. p. 90°; $n_{5893}^{15°}$ 1·4046.

(iv) *With* n-*butyl alcohol.* The (+)benzoate (5·6 g.) and *n*-butyl alcohol (6 g.) were heated on the steam-bath for 60

hrs., then dissolved in ether, and the solution washed with dilute aqueous sodium carbonate, dried, and concentrated. From the residue, two fractions were obtained: (i) *n*-butyl αγ-dimethylallyl ether (2 g.), b. p. 151—152°, $n_{5893}^{17°}$ 1·4180, $\alpha_{5461}^{20°}$ + 0·19° (*l*, 0·5); (ii) αγ-dimethylallyl benzoate (1·5 g.), b. p. 134—135°/18 mm., $n_{5893}^{17°}$ 1·4995, $\alpha_{5461}^{20°}$ + 7·71° (*l*, 0·5). Benzoic acid (2·0 g.) was isolated from the sodium carbonate washings.

Preparation of Bis-αγ-dimethylallyl Ether of High Rotatory Power.—(+)αγ-Dimethylallyl alcohol (8·6 g.), methyl *p*-toluenesulphonate (20 g.), and anhydrous potassium carbonate (20 g.) were heated on the steam-bath for 7 hrs., poured into water, and extracted with ether. From the dried, concentrated ethereal extract, two fractions were isolated: (i) (+)αγ-dimethylallyl alcohol (2 c.c.), b. p. 120·5°; (ii) *bis-αγ-dimethylallyl ether* (2 c.c.), b. p. 156—157°, $n_{5893}^{18°}$ 1·4290, $\alpha_{5461}^{20°}$ — 14·26°, $\alpha_{4358}^{20°}$ — 24·5° (*l*, 0·25) (Found: C, 77·6; H, 11·6. $C_{10}H_{18}O$ requires C, 77·8; H, 11·7%).

αγ-Dimethylallyl *p*-toluenesulphonate, formed by alkoxy-interchange, is presumably an intermediate in the formation of the ether, since no ether is formed when the alcohol is heated with anhydrous potassium carbonate only. In the absence of potassium carbonate the bis-αγ-dimethylallyl ether (b. p. 156—157°) obtained from the (+)alcohol and methyl *p*-toluenesulphonate is largely racemised (α_{5461} — 0·73°; *l*, 0·25), presumably by the concurrently formed *p*-toluenesulphonic acid.

Acid-catalysed Etherification of (−)αγ-Dimethylallyl Alcohol.—To (−)αγ-dimethylallyl alcohol (5 g.; $\alpha_{5461}^{18°}$ −0·52°, $\alpha_{4358}^{18°}$ −1·72°; *l*, 2) five drops of concentrated sulphuric acid were added, and the mixture left at room temperature for 12 hrs. It was then washed with dilute aqueous sodium carbonate, dried, and distilled, yielding bis-αγ-dimethylallyl ether (3 c.c.), b. p. 156—157°, $n_{5893}^{18°}$ 1·4374, $\alpha_{5461}^{18°}$ +0·93° (*l*, 0·25).

Optical Stability of αγ-Dimethylallyl Hydrogen Phthalate in Methyl-alcoholic Solution at 31°.—A solution of the phthalate (5·35 g.; $[\alpha]_{5461}$ +30·0° in chloroform) in methyl alcohol (100 c.c.) gave the following values for the specific rotatory power of the phthalate at room temperature: $[\alpha]_{5893}$ + 28·8°; $[\alpha]_{5780}$ + 31·1° $[\alpha]_{5461}$ + 35·5°; $[\alpha]_{4358}$ + 68·2°. These values were unchanged after the solution had been kept at 31° for 3 months.

Racemisation of αγ-Dimethylallyl Hydrogen Phthalate in Nitromethane at 31°.—A solution of the (+)phthalate (1·019 g.) in nitromethane (20 c.c.) had $\alpha_{5893}^{17°}$ + 2·48°; $\alpha_{5780}^{17°}$ + 2·72°; $\alpha_{5461}^{17°}$ +3·10°; $\alpha_{4358}^{17°}$ + 6·50°. This was kept at 31° and the rotatory powers gradually fell, after 61 days being $\alpha_{5893}^{20°}$ + 0·26°; $\alpha_{5780}^{20°}$ + 0·32; $\alpha_{5461}^{20°}$ + 0·34°; $\alpha_{4358}^{20°}$ + 0·70° (deposition of phthalic acid began at 20 days). After 61 days the solution was evaporated, leaving 0·65 g. of solid, which was separated by extraction with dry chloroform into phthalic acid (0·15 g.) and αγ-dimethylallyl hydrogen phthalate (0·44 g.), $[\alpha]_{5893}$ + 2·48°, $[\alpha]_{5461}$ + 3·16°. These results indicate that 20% of the phthalate had decomposed with liberation of phthalic acid, and the remainder underwent 90% racemisation.

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BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, April 23rd*, 1942.]

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109. *Azulenes. Part I. Synthesis of Vetivazulene.*

By ROBERT R. COATS and J. W. COOK.

Condensation of ethyl 4-*iso*propyl*cyclo*pentanone-2-carboxylate (II) with Δ^{β}-hexen-δ-one (III) by the Michael–Claisen–Robinson reaction gave a keto-ester (IV), which was converted by decarbethoxylation and then reduction into a mixture of dicyclic ketones represented by the structure (V). A pure constituent of this mixture was isolated, and its structure established. Vetivazulene (VIII) has been synthesised from the mixture (V) by ring-enlargement with diazomethane, followed by dehydrogenation with selenium.

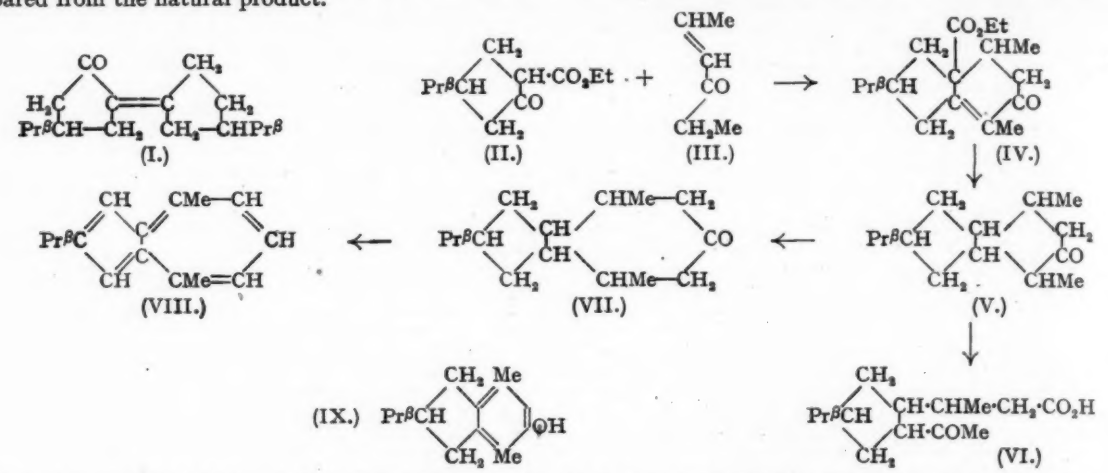
THE elucidation by St. Pfau and Plattner (*Helv. Chim. Acta*, 1936, **19**, 858; 1937, **20**, 224, 469) of the type of structure present in the blue hydrocarbons obtained by dehydrogenation of certain essential oils made it of interest to study the synthesis and chemical properties of members of this group of coloured hydrocarbons. Interest in these compounds was reinforced by the elegant analytical proof, published while the present work was in progress (St. Pfau and Plattner, *ibid.*, 1940, **23**, 768), that the dicyclic hydroazulene system is in fact present in β-vetivone, a constituent of vetiver oil (*idem, ibid.*, 1939, **22**, 640; compare Sabetay and Traband, *Bull. Soc. chim.*, 1942, **8**, 152).

It was decided in the first instance to undertake the synthesis of vetivazulene (VIII), a product of dehydrogenation of Java vetiver-oil. Our synthesis was well under way when it found that vetivazulene had already been synthesised by another method (*idem, ibid.*, 1939, **22**, 202), which, however, did not completely establish the structure. This prior work made it possible to devote less attention to the rather troublesome later stages of our synthesis than would otherwise have been necessary.

The type of method which we adopted was that developed with such success by Robinson and his collaborators (*e.g.*, Rapson and Robinson, J., 1935, 1285; du Feu, McQuillin, and Robinson, J., 1937, 53) for the synthesis of polycyclic ketones. Attempted condensation of sodio-3-*iso*propyl*cyclo*pentanone with Δ^{β}-hexen-δ-one (III) gave unsatisfactory results on account of the large proportion of 3-*iso*propyl*cyclo*pentanone converted into di*iso*propyl*cyclo*pentylidene*cyclo*pentanone (probably I) by sodamide in cold ether. Δ^{β}-Hexen-δ-one (III) condensed smoothly, however, with the sodio-derivative of ethyl 4-*iso*propyl*cyclo*pentanone-2-carboxylate (II). The resulting mixture of esters (IV) underwent successive hydrolysis and decarboxylation with boiling alcoholic potash. The ready hydrolysis of the quaternary ester and the lability of the resulting acid are unusual and must be ascribed to stereochemical influences. Hydrogenation with palladium of the unsaturated ketones so formed gave a mixture of stereoisomeric ketones (V), from which one pure component was isolated through its *semicarbazone*. Oxidation of the mixed ketones with chromic acid gave not only the β-(2-*acetyl*-4-iso*propyl*-cyclo*pentyl*)*butyric acid* (VI) formed by similar treatment of the stereochemically pure *ketone* (V), but also a stereoisomeric *keto-acid* (VI).

The m. p. of the semicarbazone of the pure ketone (V) is not very different from that of the semicarbazone

of the dimethyl*iso*propylhydrindanone obtained by St. Pfau and Plattner (*Helv. Chim. Acta*, 1940, **23**, 768) by degradation of tetrahydro-β-vetivone (VII) and it is possible that our synthetic ketone is identical with that prepared from the natural product.



It was expected that the action of diazomethane on the ketone (V) would lead to enlargement of the six-membered ring to a seven-membered ring with formation of optically inactive tetrahydrovetivone (VII) (compare Mosettig and Burger, *J. Amer. Chem. Soc.*, 1930, **52**, 3456; Adamson and Kenner, J., 1939, 181). However, the only pure compound isolated from this reaction was a ketone which was shown by analysis of its *semicarbazone* to be an isomeride rather than a homologue of (V). The isomerisation doubtless involves an inversion of configuration about the asymmetric carbon atom adjacent to the carbonyl group. Nevertheless, selenium dehydrogenation of the crude product of the action of diazomethane on the mixed ketones (V) gave in addition to 4 : 7-dimethyl-2-*iso*propyl-5-indanol (IX) a small yield of vetivazulene (VIII). The latter, which has a characteristic purple colour, was isolated as its complex with *s*-trinitrobenzene. A trimethylazulene, believed to have the substituents in the same positions as in vetivazulene, has recently been described (Schechter and Haller, *J. Amer. Chem. Soc.*, 1941, **63**, 3507).

In view of the interest attached to the synthesis of tetrahydrovetivone (VII) it is proposed to explore other possible methods for obtaining it from (V) or (VI).

Experimental.

All m. p.'s are corrected.

Ethyl 4-iso*Propyl*cyclo*pentanone-2-carboxylate* (II).—Benzene was converted successively into cumene, potassium *p*-cumenesulphonate, *p-iso*propylphenol, *p-iso*propyl*cyclo*hexanol, *β-iso*propyladipic acid, and ethyl 4-*iso*propyl*cyclo*pentanone-2-carboxylate. The sulphonation and the alkaline fusion proved very laborious when carried out on the necessary scale with laboratory apparatus. Cumene was prepared by the procedure of Meyer and Bernhauer (*Monatsh.*, 1929, **53** and **54**, 721), which proved somewhat more economical than the method of Haworth and Barker (J., 1939, 1302). After sulphonation (Gerhardt and Cahours, *Annalen*, 1841, **38**, 92; Spica, *Gazzetta*, 1879, **9**, 433) the *p*-sulphonic acid was isolated as its barium salt.

A mixture of fuming sulphuric acid (600 g.; 12% of sulphur trioxide) and concentrated sulphuric acid (400 g.) was slowly added with shaking to cumene (500 g.) below 40°. When homogeneous (1 hour), the mixture was kept for 3 hours and poured into water (4 l.), a smooth paste of calcium hydroxide (760 g.) (preferable to barium carbonate) added, and the liquid filtered. The solid was extracted with boiling water (3 l.), and the combined filtrates evaporated to 2 l. and filtered from a small sediment. A slight excess of barium chloride was added, and the barium salt collected and dried. A solution of the barium salt (500 g.) in boiling water (6 l.) was treated with potassium carbonate until just alkaline to phenolphthalein; after filtration the solution was evaporated to dryness. When the potassium salt was fused with potash at 280—300°, it gave *p-iso*propylphenol (b. p. 217—222°, m. p. 62—63°) in 50—55% yield (Paternò and Spica, *Gazzetta*, 1876, **6**, 535).

Hydrogenation of *p-iso*propylphenol over platinum-black is stated (Vavon and Callier, *Bull. Soc. chim.*, 1927, **41**, 677) to give a mixture of stereoisomeric 4-*iso*propyl*cyclo*hexanols (66%) and 4-*iso*propyl*cyclo*hexane (33%). By the use of a Raney nickel catalyst at 180° 4-*iso*propyl*cyclo*hexanol was readily obtained in 80% yield. The catalyst was prepared by addition of 50% aluminium–nickel alloy (16 g.; 100 mesh) to a stirred solution of potassium hydroxide (16 g.) in water (300 c.c.). When the initial reaction had subsided, the temperature was raised slowly to 100° and maintained until the reaction had almost ceased (2 hours.). The alkaline solution was decanted, and the catalyst washed by decantation, six times with hot water and once with alcohol. A mixture of *p-iso*propylphenol (200 g.) and this catalyst (8 g.) was introduced together with hydrogen into a high-pressure autoclave,* the pressure of hydrogen being 100 atms. at 180°. Stirring was effected with a stainless steel stirrer, the gland being lubricated with glycerol. The pressure fell rapidly to 30 atms., and was raised by the inlet of more hydrogen. When the theoretical amount had been absorbed (3 hours), the pressure remained constant and the resulting 4-*iso*propyl*cyclo*hexanol was distilled (b. p. 102—110°/15 mm.).

Oxidation of this carbinol to *β-iso*propyladipic acid with alkaline permanganate (v. Braun and Werner, *Ber.*, 1929, **62**, 1054) gave the required acid, but a better yield was obtained with 50% nitric acid catalysed by ammonium vanadate. This salt (0·2 g.) was dissolved in a mixture of concentrated nitric acid (250 c.c.) and water (125 c.c.) at 50—60°. 4-*iso*-

* We are much indebted to Professor W. M. Cumming for facilities, including the use of an autoclave, afforded at the Royal Technical College for this hydrogenation.

Propyl*cyclo*hexanol (100 g.) was added to the vigorously stirred solution at such a rate that the temperature was maintained at 50—55° without external heat (4—5 hours). The temperature was then raised to 100° for ½ hour, and the excess of water and nitric acid removed at 100° under reduced pressure. The residual β-*iso*propyladipic acid was esterified with ethyl alcohol and hydrogen chloride, and the ester distilled (135 g.; b. p. 145—165°/15 mm.).

For the Dieckmann reaction, sodium (15 g.) was atomised in dry toluene (200 c.c.), and ethyl β-*iso*propyladipate added at such a rate that the reaction could be controlled readily. The mixture was refluxed for 80 minutes (oil-bath at 120—130°), with occasional shaking, and cooled to 0°, ice-cold 10% hydrochloric acid (1 l.) added, and the whole shaken until no more solid remained. The separated toluene solution was washed with sodium carbonate solution and water, dried, and distilled. The resulting ethyl 4-*iso*propyl*cyclo*pentanone-2-carboxylate (64 g.; 65% yield) had b. p. 128—135°/15 mm., and gave an intense purple colour with alcoholic ferric chloride.

Hydrolysis of this ester (14 g.) by 4½ hours' boiling with 3N-hydrochloric acid (140 c.c.), followed by steam distillation, gave 3-*iso*propyl*cyclo*pentanone (8·5 g.), b. p. 75—80°/15 mm. Its semicarbazone had m. p. 192° (cf. Bouveault and Blanc, *Compt. rend.*, 1908, **146**, 233; **147**, 1314; Wallach, *Annalen*, 1912, **388**, 59) and its phenylhydrazone formed colourless plates, m. p. 75—76·5°.

Δ$^{\beta}$-Hexen-δ-one (III).—Oxidation of the carbinol resulting from the interaction of ethylmagnesium bromide and crotonaldehyde could not be effected by Oppenauer's method, aluminium *iso*propoxide, acetone, and benzene being used, or by chromic acid (after protection of the double bond by addition of bromine), and chromic acid oxidation of the corresponding δ-chloro-Δ$^{\beta}$-hexene (cf. Courtot and Pierron, *Bull. Soc. chim.*, 1929, **45**, 290) gave the required ketone in very poor yield. Recourse was therefore had to Blaise's method (*ibid.*, 1905, **33**, 39, 45), whereby allylzinc halide was condensed with propionitrile, and the ethyl allyl ketone isomerised by boiling dilute sulphuric acid. An attempt to improve this method by substituting allylmagnesium bromide (cf. Gilman and McGlumphy, *ibid.*, 1928, **43**, 1322) was unsuccessful. Allyl bromide was used in place of the allyl iodide used by Blaise (*loc. cit.*).

*Interaction of Sodio-3-iso*propyl*cyclo*pentanone *with Δ$^{\beta}$-Hexen-δ-one.*—A slow current of nitrogen was passed for 4 hours through a stirred suspension of powdered sodamide (3·2 g.) in 3-*iso*propyl*cyclo*pentanone (18 g.) and dry ether (60 c.c.), Δ$^{\beta}$-hexen-δ-one (8 g.) added slowly, stirring continued at room temperature for 4 hours, the mixture refluxed for 6 hours, and the product decomposed with hydrochloric acid. An ethereal extract was evaporated, unchanged ketones removed in steam, and the residue distilled at 10 mm., giving fractions (1) 7 g., b. p. 150—170°, (2) 5·1 g., b. p. 170—190°, and (3) 4 g., b. p. 190—220°. Fraction (2) gave a solid which crystallised from aqueous alcohol in white plates, m. p. 75—76°. This was evidently not a condensation product but was formed by the action of sodamide on 3-*iso*propyl*cyclo*pentanone, for the same ketone (probably I) (5 g.) was isolated when the cyclic ketone (14 g.) was stirred for an hour at — 20° with sodamide (3·9 g.) in ether (50 c.c.). This unsaturated ketone was hydrogenated over palladium-black in acetone to a saturated ketone which gave a *semicarbazone*, m. p. 161·5° (from acetone) (Found: C, 69·8; H, 10·85. $C_{10}H_{21}ON_3$ requires C, 69·6; H, 10·7%), and an oxime, m. p. 142—143·5° (from alcohol) (Found: C, 76·3; H, 11·7. Calc. for $C_{14}H_{25}ON$: C, 76·5; H, 11·65%). Wallach and Worlitzer (*Nachr. K. Ges. Wiss. Göttingen*, 1915, **1**, 17) obtained the bimolecular condensation product of 3-*iso*propyl*cyclo*pentanone by treatment with cold sodium ethoxide. They gave the m. p. as 77—78°, and obtained by hydrogenation a saturated ketone of which the oxime had m. p. 136°.

Condensation of Ethyl 4-iso*Propyl*cyclo*pentanone-2-carboxylate* (II) *with Δ$^{\beta}$-Hexen-δ-one* (III).—To the thick paste of sodio-compound obtained by adding the keto-ester (130 g.) to a solution of sodium ethoxide (12 g. of sodium in 650 c.c. of absolute alcohol distilled over quicklime) was added a solution of Δ$^{\beta}$-hexen-δ-one (50 g.) in absolute alcohol (200 c.c.). The whole was kept at room temperature for 60 hours (most of the solid had dissolved after 12 hours), the solution then heated, much of the alcohol (650 c.c.) distilled, and the residual solution poured into ice and water and extracted with ether. The aqueous alkaline solution was acidified, and the precipitated oil separated into fractions soluble in sodium carbonate (this was essentially *iso*propyladipic acid and gave 12 g. of ethyl ester when esterified) and in sodium hydroxide (this fraction gave an intense purple colour with ferric chloride and was apparently unchanged keto-ester). The ethereal extract of neutral product, which gave no colour with alcoholic ferric chloride, was distilled at 12 mm. into fractions (i) 14 g., b. p. 120—170°, and (ii) 70 g., b. p. 170—190°.

Fraction (ii), consisting of the dicyclic keto-ester (IV), was hydrolysed by 6 hours' boiling with alcohol (400 c.c.) and potassium hydroxide (50 g. in 35 c.c. of water), potassium carbonate separating. Some of the alcohol was distilled off, and the solution diluted with water and extracted with ether. The alkaline solution gave very little product on acidification. The ethereal extract was distilled and gave a yellowish liquid (43 g.), b. p. 160—170°/14 mm. This was essentially the unsaturated ketone formed by decarbethoxylation of (IV), but it yielded no crystalline derivatives.

Hydrogenation of this material, dissolved in alcohol (250 c.c.), over palladium-black (0·5 g.) was complete in 25 hours (hydrogen absorption, 4·2 l.). Treatment of an aqueous-alcoholic solution of the resulting saturated ketones (V) with semicarbazide, followed by crystallisation from alcohol, gave 7·2 g. of pure *semicarbazone*, which formed colourless leaflets, m. p. 204—205° (Found: C, 68·4; H, 10·2; N, 15·7. $C_{15}H_{27}ON_3$ requires C, 68·0; H, 10·3; N, 15·85%). The *oxime*, prepared from another portion of the mixed saturated ketones by heating with hydroxylamine hydrochloride in pyridine, formed fine white needles, m. p. 154·5° (Found: C, 75·1; H, 10·9. $C_{14}H_{25}ON$ requires C, 75·3; H, 11·3%).

The liquor from which the pure semicarbazone had been isolated gave only resinous material on dilution with water. This consisted of a semicarbazone mixture, from which the ketones were regenerated by steam-distillation with 20% sulphuric acid. The resulting ketone mixture was used in some experiments described below. The poor yield of pure semicarbazone hindered the subsequent stages of the synthesis, and the yield was not improved in other experiments in which the conditions of interaction of (II) and (III) were somewhat modified.

Stereochemically Pure 4 : 7-*Dimethyl*-2-iso*propyl*-5-*hydrindanone* (V).—The pure semicarbazone, m. p. 204°, was hydrolysed by steam-distillation with 20% sulphuric acid (200 c.c.). The regenerated ketone was extracted from the steam-distillate with ether, and the extract dried (sodium sulphate) and evaporated on the water-bath. The pure *ketone*, distilled at 0·3 mm. from an air-bath at 100°, formed a colourless liquid with a feeble peppermint odour, and had $d_4^{19°}$ 0·9419 and $n_D^{16°}$ 1·4778; whence $[R_L]_D$ = 62·52 (calc., 62·70) (Found: C, 80·4; H, 11·7. $C_{14}H_{24}O$ requires C, 80·7; H, 11·6%). Reconversion of this ketone into the same semicarbazone from which it was prepared showed that the sulphuric acid used for hydrolysis did not effect configurational change. A crystalline benzylidene derivative was not obtained from this ketone.

Dehydrogenation of the pure ketone (1 g.) with palladium-black (0·1 g.) was effected by heating for 9 hours at 290—300° in an evacuated sealed tube. The resulting 4 : 7-dimethyl-2-*iso*propyl-5-indanol (IX) (0·25 g.), isolated by digestion with light petroleum, in which it was sparingly soluble, crystallised from hexane in colourless needles, m. p. 133—134° (Found: C, 81·9; H, 9·5. Calc. for $C_{14}H_{20}O$: C, 82·3; H, 9·9%) (St. Pfau and Plattner, *Helv. Chim. Acta*, 1940, **23**, 792, give m. p. 129—130°). This dehydrogenation product had the character of a cryptophenol (cf. Farinholt, Harden, and Twiss, *J. Amer. Chem. Soc.*, 1933, **55**, 3383). It gave a 3 : 5-*dinitrobenzoate*, which crystallised from alcohol in fine, colourless needles, m. p. 145—146° (Found: C, 63·6; H, 5·8; N, 7·4. $C_{21}H_{22}O_6N_2$ requires C, 63·3; H, 5·6; N, 7·0%).

*β-(2-Acetyl-4-iso*propyl*cyclo*pentyl)butyric Acid* (VI).—A solution of the pure ketone (V) (0·5 g.) in glacial acetic acid was treated with a concentrated aqueous solution of chromic acid (0·2 g.). The solution was warmed to 75° and then allowed to cool slowly. The acidic oxidation product gave a *semicarbazone* ((0·15 g.) which crystallised from alcohol in

short colourless needles, m. p. 181—182° (Found: C, 60·9; H, 9·2; N, 14·3. $C_{15}H_{27}O_3N_3$ requires C, 60·5; H, 9·1; N, 14·1%).

Hydrolysis of this semicarbazone (1·5 g.) by aqueous sulphuric acid in boiling alcohol, followed by alkaline hydrolysis of the ester, gave colourless slender needles, m. p. 64—65° (from hexane), consisting of *β*-(2-*acetyl*-4-iso*propyl*cyclo*pentyl*)-*butyric acid* (VI) (Found: C, 69·9; H, 10·2. $C_{14}H_{24}O_3$ requires C, 69·9; H, 10·1%). Its p-*phenylphenacyl* ester formed colourless leaflets (from alcohol), m. p. 75—76° (Found: C, 77·8; H, 7·9. $C_{33}H_{34}O_4$ requires C, 77·8; H, 7·7%).

Examination of Crude Mixture of Stereoisomeric Dicyclic Ketones (V).—The material recovered by steam-distillation with 20% sulphuric acid of the mixture present in liquors from which the semicarbazone, m. p. 204°, had been isolated (see above) was treated with chromic acid with the object of oxidising any hydroxylic compounds present. For this purpose a solution of chromic acid (20 g.) in 80% acetic acid (50 c.c.) was added to a solution of the oil in glacial acetic acid (250 c.c.). The temperature rose slowly to 45°. After being kept overnight, the solution was poured into water and extracted with ether. By shaking the extract with sodium carbonate solution there was removed some acidic oxidation product, isolated as a yellow gum (8 g.). This gave a solid mixture of semicarbazones (6 g.), which was separated by fractional crystallisation from alcohol into the semicarbazone (2·6 g.), m. p. 181°, of the substituted butyric acid (VI) already described, and a more soluble *semicarbazone*, m. p. 151—155°, of an isomeric keto-acid. This crystallised from alcohol in colourless leaflets (2 g.) (Found: C, 60·8; H, 9·2%) and was hydrolysed to a keto-acid which formed a gum. This gave a p-*phenylphenacyl* ester, which crystallised from methyl alcohol in colourless microscopic leaflets, m. p. 66—67° (Found: C, 77·3; H, 7·9%). The m. p. was slightly but definitely depressed by the stereoisomeric ester, m. p. 75°. As one of the three substituents in the *cyclo*pentane ring is an acetyl group, it is unlikely that there would be more than two optically inactive stable forms of the keto-acid (VI). In the case of the dicyclic ketone (V) the number of possible stereoisomerides is considerable.

The neutral fraction recovered from this oxidation experiment formed a yellow oil (25 g.), b. p. 145—155°/12 mm. Crystalline semicarbazones could not be obtained from it, and it was resistant to hydrogenation over platinum-black. This material was used for subsequent stages of the synthesis.

Action of Diazomethane on 4 : 7-*Dimethyl*-2-iso*propyl*-5-*hydrindanone* (V).—(i) In view of the finding of Adamson and Kenner (*loc. cit.*) that ethereal diazomethane reacts exceedingly slowly with 2-methyl*cyclo*hexanone we adopted in the first instance the experimental conditions which enabled these workers to obtain 2- and 3-methyl*cyclo*heptanone. Anhydrous potassium carbonate (0·1 g.) was added to a solution of the pure dicyclic ketone (V) (2 g.) in absolute alcohol (2 c.c.). Nitrosomethylurethane (1·4 g.) was added during 3 days, the mixture being kept at 0°. After 2 further days the alcohol was removed from the filtered solution. The resulting oil, which, like the original ketone, did not react with sodium bisulphite, was treated with semicarbazide hydrochloride and sodium acetate in cold aqueous alcoholic solution. The resulting crystalline product was not homogeneous, but by crystallisation from alcohol there was readily isolated a *semicarbazone* in well-formed colourless needles, m. p. 167—168° (Found: C, 67·9, 68·1, 68·7; H, 10·1, 10·2, 10·15; N, 15·6, 15·9. $C_{15}H_{27}ON_3$ requires C, 68·0; H, 10·3; N, 15·85%. $C_{16}H_{29}ON_3$ requires C, 68·8; H, 10·5; N, 15·0%). These analyses, carried out on two different specimens of the semicarbazone, suffice to show that isomerisation rather than ring-enlargement had taken place.

(ii) Methyl alcohol (9 c.c.) was added to a solution of the pure ketone (V) (2 g.) in ethereal diazomethane (from 3 c.c. of nitrosomethylurethane, 35 c.c. of ether, and 3·6 c.c. of 25% methyl-alcoholic potassium hydroxide). Slow liberation of nitrogen set in and after 48 hours this had almost ceased and the solution was nearly colourless. The oil remaining after removal of the solvents gave a semicarbazone (2·7 g.), m. p. 145—150°. A pure component could not be obtained from this by fractional crystallisation. An unsuccessful attempt was made to obtain a crystalline dibenzylidene derivative from the ketone mixture formed from this by hydrolysis with 20% sulphuric acid (tetrahydro-*β*-vetivone gives such a derivative).

(iii) The neutral oil recovered from the oxidation of the mixture of ketones (V) (20 g.) was treated with diazomethane for 5 days at room temperature, as described under (ii). Ketonic material (11 g.) was separated from the product by means of Girard's reagent T. Treatment of some of this (5 g.) with semicarbazide gave a resinous mixture of semicarbazones, an alcoholic solution of which deposited crystals (0·5 g.) on long standing. These consisted of the semicarbazone, m. p. 167—168°, described under (i).

Vetivazulene (VIII).—Although tetrahydro-*β*-vetivone (VII) or a stereoisomeride was not isolated from the foregoing experiments with diazomethane, the presence in the mixed products of a compound of this structure was shown by dehydrogenation. The ketonic material obtained as described in the previous paragraph (5 c.c.) was heated with selenium (10 g.) at 280—310° for 24 hours. The product was extracted with ether and distilled at 10—11 mm. from a bath slowly heated from 155° to 190°, the final fractions being taken off at 0·1 mm. The violet distillate, which was partly crystalline, was treated with hexane and gave crystals of 4 : 7-dimethyl-2-*iso*propyl-5-indanol (IX) (0·75 g.). The violet hexane liquors were diluted with hexane, and the solution passed through a column of alumina. The violet zone was separated and eluted with alcohol, the solvent mostly evaporated, and the concentrated solution treated with *s*-trinitrobenzene (100 mg.). The crystalline product, recrystallised from alcohol, formed reddish-brown needles, m. p. 150—151·5°. This was the complex of vetivazulene (VIII), for which St. Pfau and Plattner (*Helv. Chim. Acta*, 1936, **19**, 871; 1939, **22**, 207) give m. p. 151·5° (Found: C, 61·5; H, 5·3; N, 10·3. Calc. for $C_{15}H_{18}.C_6H_3O_6N_3$: C, 61·3; H, 5·15; N, 10·2%).

The analyses were all micro-analyses carried out by Mr. J. M. L. Cameron. We thank the Carnegie Trust for a scholarship which enabled one of us (R. R. C.) to take part in this work.

UNIVERSITY OF GLASGOW. [*Received, May 8th*, 1942].

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110. *Acenaphthene Series. Part I. Mono- and Di-*tert.*-butyl-acenaphthene, -acenaphthenequinone, and -naphthalic Anhydride, and their Derivatives.*

By ARNOLD THORNTON PETERS.

3-tert.-*Butylacenaphthene* (I), prepared by the Friedel–Crafts reaction from acenaphthene, is oxidised to 4-tert.-*butylnaphthalic anhydride* (III), which condenses with *o*-phenylenediamine to yield 9′-*keto*-3′(or 4′)-tert.-*butyl*-8′-*azaphenalino*-(7′ : 8′ : 2 : 3)-*ψ-indole* (as VI). Controlled oxidation of (I) affords (III) and 12% of 3-tert.-*butylacenaphthenequinone* (IV). 3 : 4-*Di*-tert.-*butylacenaphthene* (II) is oxidised to 4 : 5-*di*-tert.-*butylnaphthalic anhydride* (V), or to a double compound (VII) of the anhydride (V) and 3 : 4-*di*-tert.-*butylacenaphthenequinone*, from which the pure quinone is liberated by the novel method of repeated extraction with 10% aqueous sodium carbonate at 170° under pressure. Many derivatives are prepared; *e.g.*, 3′ : 4′-*di*-tert.-

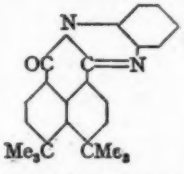
butyl*-1 : 7′-*thionaphthenacenaphthenylindigo **(VIII), which dyes cotton magenta-red from an alkaline hydrosulphite vat.**

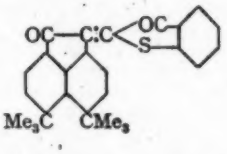
THE object of this research was to obtain oriented higher alkyl derivatives of acenaphthene, acenaphthenequinone, and naphthalic anhydride, and to investigate their use as intermediates for vat dyes.

3-tert.-*Butyl*-(I) and 3 : 4-*di*-tert.-*butyl-acenaphthene* (II) are prepared from acenaphthene (1 mol.) and *tert.*-butyl chloride (1 and 1·8 mols., respectively) in carbon disulphide, only 0·2 mol. of aluminium chloride being used. In preparing (II), small amounts of (I) are always formed, but the use of relatively larger amounts of *tert.*-butyl chloride produces more resinous material. 3-*tert.*-Butylacenaphthene is oxidised by sodium dichromate in acetic acid to 4-tert.-*butylnaphthalic anhydride* (III), which affords an *imide*, N-*methylimide*, and *phenylhydrazide*, and condenses with *o*-phenylenediamine in acetic acid to yield 9′-*keto*-3′(or 4′)-tert.-*butyl*-8′-*azaphenalino*-(7′ : 8′ : 2 : 3)-ψ-*indole* (as VI). A carefully controlled oxidation of (I) affords (III) together with 12% of 3-tert.-*butylacenaphthenequinone* (IV), which condenses with 2-hydroxythionaphthen in a mixture of acetic and hydrochloric acids (5 : 1) to give the brilliant scarlet 3′ (or 4′)-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo*; this stains cotton pink from a difficultly formed alkaline hydrosulphite vat. Unlike acenaphthenequinone, (IV) is only sparingly soluble in boiling aqueous sodium bisulphite, and even after extraction with boiling aqueous sodium carbonate in an open vessel or under pressure at 150°, followed by fractional crystallisation, and then chromatographic analysis, complete purification was not effected.

3 : 4-Di-*tert.*-butylacenaphthene (II) is oxidised to 4 : 5-*di*-tert.-*butylnaphthalic anhydride* (V), which yields an *imide*, N-*methylimide*, and 9′-*keto*-3′ : 4′-*di*-tert.-*butyl*-8′-*azaphenalino*-(7′ : 8′ : 2 : 3)-ψ-*indole* (VI). An unusual product resulted from a carefully controlled oxidation of (II) with sodium dichromate and acetic acid at 95—105° for 15 minutes; after separation of the anhydride (V), the residue crystallised in golden-yellow needles, m. p. 186°, of a double compound (VII) of equimolecular proportions of 3 : 4-*di*-tert.-*butylacenaphthenequinone* and 4 : 5-*di*-tert.-*butylnaphthalic anhydride*, unchanged by crystallisation from nitrobenzene, pyridine or quinoline, or by chromatographic analysis. The pure *quinone* is obtained with difficulty after several extractions of (VII) with 10% aqueous sodium carbonate at 170° in a sealed tube, and is reconvertible into (VII). Quantitative experiments were carried out by condensing (VII) with phenylhydrazine; 3 : 4-*di*-tert.-*butylacenaphthenequinonediphenylhydrazone* was then separated from the *phenylhydrazide* of (V). Similarly, condensation of (VII) with 2-hydroxythionaphthen caused reaction with the 3 : 4-di-*tert.*-butylacenaphthenequinone to give 3′ : 4′-*di*-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo* (VIII) and the unreacted anhydride (V) was recovered. Compound (VIII) dyes cotton magenta-red from an orange-brown alkaline hydrosulphite vat, and 5-*ethoxy*-3′ : 4′-*di*-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo* dyes cotton reddish-orange from a yellow vat.

(VI.)





(VIII.)

Attempted oxidation of the *tert.*-butyl groups to carboxyl in compounds (III) and (V) by chromic acid, alkaline permanganate or hydrogen peroxide, or dilute nitric acid, under various conditions, yielded either unchanged material or resins. There is little doubt that the stated orientations for the *tert.*-butylacenaphthenes are correct, by analogy with the ethyl analogues (Mayer and Kaufmann, *Ber.*, 1920, **53**, 289), and this is supported by the known reactivity of positions 3 and 4 in acenaphthene; *e.g.*, 3-acetyl- and -propionyl-, and 3 : 4-diacetyl- and -dipropionyl-acenaphthene are obtained by the Friedel–Crafts reaction (Dziewónski and collaborators, *Bull. Acad. Polonaise*, 1931, *A*, 232, 242).

EXPERIMENTAL.

The m. p.'s are corrected. Microanalyses were carried out by Dr. G. Weiler and Dr. F. B. Strauss, of Oxford.

3-tert.-*Butylacenaphthene*.—Anhydrous aluminium chloride (13·4 g.; 0·2 mol.) was added during 1 hour to a well-stirred mixture of acenaphthene (77 g.; 1 mol.) and *tert.*-butyl chloride (46·25 g.; 1 mol.) in dry carbon disulphide, the mixture refluxed for 2 hours, and ice-water (400 g.) and concentrated hydrochloric acid (60 c.c.) then added. The solvent layer was separated, the aqueous layer extracted with carbon disulphide, the combined extracts dried (sodium sulphate), and the solvent removed. The residue was distilled and the fraction, b. p. 310—325°, was recrystallised from aqueous alcohol, 3-tert.-*butylacenaphthene* separating in colourless prisms, m. p. 73—74°, b. p. 170—174°/7 mm. (yield, 56 g.; 53·3%) (Found: C, 91·4; H, 8·6. $C_{16}H_{18}$ requires C, 91·4; H, 8·6%). It is accompanied by unchanged acenaphthene and some di-*tert.*-butylacenaphthene; traces of the latter are difficult to remove and successive distillation and fractional crystallisation are necessary to obtain a pure specimen.

The *picrate* separated in orange-red needles, m. p. 86—90° (Found: N, 9·8. $C_{16}H_{18},C_6H_3O_7N_3$ requires N, 9·6%), readily decomposed on heating with organic solvents.

4-tert.-*Butylnaphthalic Anhydride*.—Sodium dichromate (45 g.) was added to a solution of 3-*tert.*-butylacenaphthene (15 g.) in acetic acid (400 c.c.), and the mixture refluxed for 40 minutes. After addition to ice-water (600 g.), the precipitate was collected and extracted repeatedly with boiling 15% aqueous sodium carbonate; the cooled, charcoaled, combined extracts were acidified, and the precipitate refluxed with acetic acid for 10 minutes. The *anhydride* crystallised from dilute acetic acid in colourless needles, m. p. 201—202° (yield, 13 g.; 71·7%) (Found: C, 75·6; H, 5·4. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%).

Derivatives. On refluxing with excess of aqueous ammonia (*d* 0·88) and a little alcohol for 20 minutes, the anhydride afforded 4-tert.-*butylnaphthalimide*, which crystallised from methyl alcohol in colourless needles, m. p. 256° (Found:

C, 76·1; H, 6·0; N, 6·0. $C_{16}H_{13}O_2N$ requires C, 75·9; H, 5·9; N, 5·5%). 33% Aqueous methylamine similarly yielded the N-*methylimide*, which crystallised from alcohol in colourless silky needles, m. p. 173° (Found: N, 5·4. $C_{17}H_{15}O_2N$ requires N, 5·2%). The *phenylhydrazide* crystallised from aqueous acetic acid in yellow prisms, m. p. 187—188° (Found: N, 8·0. $C_{22}H_{20}O_2N_2$ requires N, 8·1%). The anhydride (1 mol.) and *o*-phenylenediamine (1·4 mols.), refluxed in acetic acid for 10 minutes, afforded 9′-*keto*-3′ (or 4′)-tert.-*butyl*-8′-*azaphenalino*-(7′ : 8′ : 2 : 3)-*ψ*-*indole*, which separated from aqueous acetic acid in greenish-yellow prismatic needles, m. p. 194—195° (Found: C, 81·0; H, 5·3; N, 8·8. $C_{22}H_{16}ON_2$ requires C, 81·0; H, 5·5; N, 8·6%), soluble in alcohol or acetic anhydride with a yellow colour and slight green fluorescence, and in cold concentrated sulphuric acid with an orange colour. The usual intense fluorescence, due to naphthafluorescein formation, was observed when the fusion mixture of the anhydride, resorcinol, and zinc chloride was added to dilute ammonia solution.

3-tert.-*Butylacenaphthenequinone*.—Sodium dichromate (45 g.) was added all at once to a solution of specially purified 3-*tert*.-butylacenaphthene (15 g.) in acetic acid (400 c.c.) at 95°, and the mixture heated to 105°; the reaction was then allowed to proceed without external heating until it subsided (7 minutes). Ice-water (600 g.) was added, and the yellow precipitate (*A*) (14·5 g.) washed with warm water and extracted seven times with boiling 15% aqueous sodium carbonate (500 c.c.) for 20 minutes; the combined extracts were acidified and the colourless precipitate was boiled with acetic acid and crystallised to give 4-*tert*.-butylnaphthalic anhydride, m. p. and mixed m. p. 201—202° (yield, 5·5 g.; 30·3%). The residue was fractionally crystallised from aqueous alcohol, and the fractions tested by condensing with 2-hydroxythionaphthen. The resulting yellow needles, rich in quinone, were extracted repeatedly with boiling 15% aqueous sodium carbonate, and the residue was crystallised repeatedly from aqueous acetic acid and finally from aqueous alcohol, forming pale yellow needles, m. p. *ca.* 156—159°, of 3-tert.-*butylacenaphthenequinone* (yield, 1·6 g.; 9·4%) (Found: C, 80·8; H, 5·8. $C_{16}H_{14}O_2$ requires C, 80·7; H, 5·9%).

Condensation of product (*A*) (0·87 g.) with freshly prepared 2-hydroxythionaphthen (0·7 g.) in a mixture of acetic and hydrochloric acids (5 : 1) yielded 3′-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo* [0·19 g., equivalent to 14% of 3-*tert*.-butylacenaphthenequinone in the product (*A*)], which separated from acetic acid in brilliant scarlet prismatic needles, m. p. 300—301° (Found: C, 78·3; H, 5·4; S, 8·2. $C_{34}H_{16}O_2S$ requires C, 77·8; H, 4·9; S, 8·65%). It dissolved in cold concentrated sulphuric acid with a deep bluish-green colour, becoming bluish-red on dilution.

3 : 4-*Di*-tert.-*butylacenaphthene*.—This was prepared in the same way as the 3-*tert*.-butyl compound, 83·3 g. (1·8 mols.) of *tert*.-butyl chloride being used. The residue was distilled, and the fraction, b. p. 335—365°/760 mm., collected, leaving a resin which, if not removed, hindered subsequent crystallisation. 3 : 4-*Di*-tert.-*butylacenaphthene* crystallised from alcohol in colourless plates or more slowly in colourless prismatic needles, or from acetic acid in long, colourless, prismatic needles, m. p. 162—163°, b. p. 358—360°/758 mm. (yield, 87 g.; 72·7%, calc. on *tert*.-butyl chloride) (Found: C, 90·2; H, 9·6. $C_{20}H_{26}$ requires C, 90·2; H, 9·8%), soluble in cold benzene, acetone, chloroform, light petroleum or ether. It afforded a red micro-crystalline *picrate*, m. p. 164° (Found: N, 8·75. $C_{20}H_{26}.C_6H_3O_7N_3$ requires N, 8·5%), decomposed in hot dry alcohol, chloroform, or light petroleum.

4 : 5-*Di*-tert.-*butylnaphthalic Anhydride*.—Sodium dichromate (40 g.) was added during 15 minutes to a solution of 3 : 4-di-*tert*.-butylacenaphthene (10 g.) in acetic acid (300 c.c.) at 110°, and the mixture refluxed for 1 hour. After addition to ice-water (500 g.), the almost colourless precipitate was collected and washed with water. 4 : 5-*Di*-tert.-*butylnaphthalic anhydride* crystallised from acetic acid or alcohol in colourless fine needles, or in rhombohedra, m. p. 211°, both forms often separating simultaneously (Found: C, 77·4; H, 6·95. $C_{20}H_{22}O_3$ requires C, 77·4; H, 7·1%).

Derivatives. 4 : 5-*Di*-tert.-*butylnaphthalimide* crystallised from alcohol in colourless needles, m. p. 240° (Found: N, 4·6. $C_{20}H_{23}O_2N$ requires N, 4·5%), the N-*methylimide* in long colourless needles, m. p. 231—232° (Found: C, 78·4; H, 7·6; N, 4·2. $C_{21}H_{25}O_2N$ requires C, 78·0; H, 7·7; N, 4·3%), which gave a violet fluorescence in alcohols, the *phenylhydrazide* in pale yellow prisms, m. p. 246° (Found: C, 78·0; H, 6·8; N, 7·0. $C_{26}H_{28}O_2N_2$ requires C, 78·0; H, 7·0; N, 7·0%), and the *oxime* in colourless prisms, m. p. 180° (Found: N, 4·2. $C_{20}H_{23}O_3N$ requires N, 4·3%). 9′-*Keto*-3′ : 4′-*di*-tert.-*butyl*-8′-*azaphenalino* (7′ : 8′ : 2 : 3)-*ψ*-*indole* (VI), prepared similarly to the mono-*tert*.-butyl compound (see above), crystallised from acetic acid in greenish-yellow prismatic needles, m. p. 278—279° (Found: C, 81·7; H, 6·5; N, 7·7. $C_{36}H_{36}ON_2$ requires C, 81·7; H, 6·8; N, 7·3%), which dissolved in alcohol with a yellow colour and a green fluorescence; a similar but less marked fluorescence appeared in acetic anhydride, from which solvent the product could be recrystallised unchanged. It dissolved in cold concentrated sulphuric acid with an orange colour. 4 : 5-Di-*tert*.-butylnaphthalic anhydride is recovered unchanged on melting with *p*-nitroaniline, or on boiling with a solution of 2-hydroxythionaphthen in aqueous alcohol containing potassium carbonate or in a mixture of acetic and hydrochloric acids (5 : 1).

Double Compound of 3 : 4-*Di*-tert.-*butylacenaphthenequinone and* 4 : 5-*Di*-tert.-*butylnaphthalic Anhydride*. *Preparation of* 3 : 4-*Di*-tert.-*butylacenaphthenequinone*.—The oxidation of 3 : 4-di-*tert*.-butylacenaphthene (15 g.) with sodium dichromate was carried out similarly to that of the 3-*tert*.-butyl compound. The sodium carbonate extracts of the yellow solid (13 g.) obtained gave on acidification an almost colourless solid, which crystallised from acetic acid in almost colourless, fine needles or rhombohedra of 4 : 5-di-*tert*.-butylnaphthalic anhydride (4 g.). The residue from the alkali extractions was extracted with 15% aqueous sodium bisulphite (300 c.c.) on the water-bath for 20 minutes, and the extract boiled with dilute sulphuric acid for 20 minutes to yield a yellow solid (*B*, 0·3 g.), m. p. 186°. The insoluble residue, recrystallised from acetic acid, formed large, yellow, prismatic needles, or, from alcohol, long silky needles, of constant m. p. 186°, identical with (*B*). The compound appeared homogeneous under the microscope, and is a double *compound* of equimolecular proportions of 3 : 4-di-*tert*.-butylacenaphthenequinone and 4 : 5-di-*tert*.-butylnaphthalic anhydride (Found: C, 79·4, 79·6; H, 7·3, 7·3. $C_{20}H_{22}O_2.C_{20}H_{22}O_3$ requires C, 79·5; H, 7·3%). The m. p. was not depressed by either the pure quinone or the anhydride. After chromatographic analysis (alumina; light petroleum or benzene) the compound still had m. p. and mixed m. p. 186° (Found: C, 79·4; H, 7·2%). It dissolved in warm alcoholic potassium hydroxide with a green colour, with partial decomposition of the quinone. The quinone could not be separated *via* the hydrazone or oxime, but after the double compound (1 g.) had been extracted three times with 10% aqueous sodium carbonate in a sealed tube at 170° for 3 hours, the insoluble residue crystallised from alcohol in yellow silky needles (0·3 g.), m. p. 213—214°, of 3 : 4-*di*-tert.-*butylacenaphthenequinone* (mixed m. p. with 4 : 5-di-*tert*.-butylnaphthalic anhydride 182—186°) (Found: C, 81·7; H, 7·2. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%). A mixture of equimolecular proportions of the quinone and the anhydride on crystallisation from alcohol gave yellow needles, m. p. and mixed m. p. with the double compound 185—186°.

Derivatives of 3 : 4-*Di*-tert.-*butylacenaphthenequinone*.—These were most conveniently prepared from the double compound, m. p. 186°, which had been recrystallised until the m. p. was constant for three successive crystallisations.

The compound (VII) (0·25 g.) in 90% aqueous acetic acid (7 c.c.) was refluxed with phenylhydrazine (0·3 g.) in the same solvent (5 c.c.) for 10 minutes. After cooling to 50°, the orange crystals were collected and recrystallised from acetic acid, forming orange-red needles, m. p. 240—242°, of 3 : 4-*di*-tert.-*butylacenaphthenequinonediphenylhydrazone* (yield, 0·11 g.; 56%) (Found: C, 79·8; H, 7·5: N, 11·7. $C_{32}H_{34}N_4$ requires C, 80·4; H, 7·2; N, 11·8%). The mother-liquors yielded pale yellow prisms, m. p. and mixed m. p. with the phenylhydrazide of 4 : 5-di-*tert*.-butylnaphthalic anhydride, 246° (yield, 0·09 g.; 53%); 0·1 g. of a mixture, m. p. 200°, of the hydrazone and the hydrazide was also obtained, and the m. p. was not depressed on admixture with a synthetic mixture.

An analytical specimen of 3′ : 4′-*di*-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo* (VIII), prepared by condensation of (VII) and 2-hydroxythionaphthen in a mixture of acetic and hydrochloric acids (5 : 1), crystallised from acetic acid in bluish-red prismatic needles, m. p. 260—262° (Found : C, 78·7; H, 6·1; S, 7·2. $C_{28}H_{26}O_2S$ requires C, 78·9; H, 6·1; S, 7·5%). 2-Hydroxythionaphthen and its analogues are slightly decomposed in aqueous-alcoholic alkali, though the latter medium is useful in preparing large amounts of dye. The dye dissolves in cold concentrated sulphuric acid with a deep green colour, becoming wine-red on dilution.

5-*Ethoxy*-3′ : 4′-*di*-tert.-*butyl*-1 : 7′-*thionaphthenacenaphthenylindigo* crystallised from acetic acid in fine orange-red needles, m. p. 262—265° (Found : C, 76·1; H, 6·1; S, 6·5. $C_{30}H_{30}O_3S$ requires C, 76·6; H, 6·4; S, 6·8%), which dissolved in cold concentrated sulphuric acid with a brownish-violet colour, becoming salmon-coloured on dilution.

3 : 4-*Di*-tert.-*butylacenaphthenequinone*-p-*nitrophenylhydrazone* crystallised from acetic acid in orange prismatic needles, m. p. 285—287° (Found : C, 72·8; H, 6·1; N, 10·1. $C_{26}H_{27}O_3N_3$ requires C, 72·7; H, 6·3; N, 9·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised in deep orange needles, m. p. 324° (Found : C, 65·7; H, 5·6; N, 11·7. $C_{26}H_{26}O_5N_4$ requires C, 65·8; H, 5·5; N, 11·8%), converted by refluxing with excess of 2 : 4-dinitrophenylhydrazine in acetic acid for 2 hours into the *bis*-2 : 4-*dinitrophenylhydrazone*, which separated in orange-red prisms, m. p. 320° (Found : N, 16·3. $C_{32}H_{30}O_8N_8$ requires N, 17·1%).

The author thanks Imperial Chemical Industries (Dyestuffs), Ltd., for a gift of acenaphthene.

CLOTHWORKERS' RESEARCH LABORATORY, LEEDS UNIVERSITY. [*Received, May 15th*, 1942.]

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111. *The Electric Polarisation of Mercurous Trichloroacetate and of Quinol Bistrichloroacetate.*

By N. R. DAVIDSON and L. E. SUTTON.

Mercurous trichloroacetate is soluble in benzene. In order to discover whether this is due to any peculiarity in the structure of the solute molecule, its electric polarisation in this solvent has been determined at 25° and compared with that of *quinol bistrichloroacetate*, with which there might be a structural similarity if the O–Hg–Hg–O atoms are collinear in the former.

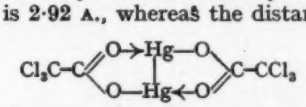
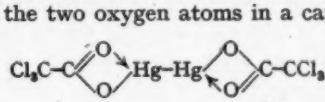
The apparent electric dipole moments are 2·65 ± 0·10 and 1·50 ± 0·20 D., respectively, the uncertainties being due to atom polarisation. The large value for the former excludes any rigid chelate structures and favours the simple covalent one $Cl_3C{\cdot}C\langle{}^{O}_{O-Hg-Hg-O}\rangle{}^{O}C{\cdot}CCl_3$ in which the trichloroacetyl groups are free to rotate about the O–Hg–Hg–O axis : the difference between the moments of this and of the quinol ester may reasonably be attributed to the effects of resonance.

THE number of chemical compounds which contain a metal and are appreciably soluble in organic solvents is relatively small. Apart from organo-metallic compounds proper, in which the metal atom is directly bound to a carbon atom, most of the members of the class are chelate compounds in which the covalent bonding is stabilised by resonance, and frequently the solubility in non-polar solvents is increased by the presence of large organic addenda. The solubility of silver perchlorate in benzene is apparently an isolated and unexplained case.

The observation by Bateman and Conrad (*J. Amer. Chem. Soc.*, 1915, **37**, 2559) that mercurous trichloroacetate is soluble in benzene is therefore of considerable interest, and in an effort to throw further light on the structure of this compound we have investigated its molecular weight and electric polarisation in benzene solution. Since our work was completed, Swarts (*Bull. Soc. chim. Belg.*, 1939, **48**, 176) has reported that mercurous trifluoroacetate is also soluble in benzene.

As was anticipated, cryoscopic measurements showed that the molecular formula of mercurous trichloroacetate is $Hg_2(C_2O_2Cl_3)_2$. Swarts's ebullioscopic measurements give a dimeric formula for the trifluoroacetate. In every known case of a mercurous compound, whether in ionic aqueous solution, in the gas phase, or as a solid, two mercury atoms are linked together (cf. Latimer and Hildebrand, " Reference Book of Inorganic Chemistry," The Macmillan Co., New York, 1933, p. 109), so it is reasonable to assume that the dimerisation of the trichloroacetate involves the formation of an Hg–Hg link.

The results of the electric polarisation measurements are : $P_2 = 245{\cdot}7 \pm 1$ c.c., $_EP_2 = 79{\cdot}5 \pm 2$ c.c., whence $P_{A+O} = 166 \pm 3$ c.c. It is clear that a compound with such a large value of P_{A+O} must have a permanent dipole moment and hence an unsymmetrical structure. Whatever the structure, there is a large number of polar groups in the molecule, so that we may expect (Coop and Sutton, J., 1938, 1269) a large atom polarisation; if P_A is 30 c.c., $\mu = 2{\cdot}56$ D.; if P_A is 6 c.c., μ is 2·78 D. We take $\mu = 2{\cdot}65 \pm 0{\cdot}10$ D.* A symmetrical chelate structure (I) for this compound, besides being incompatible with the observed moment, is stereochemically unlikely. If the mercury radius is the same as that in covalent mercuric compounds, the Hg–Hg distance is 2·92 A., whereas the distance between the two oxygen atoms in a carboxyl group is only

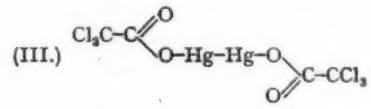
(I.)  (II.) 

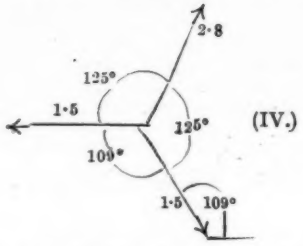
about 2·4 A.; hence a considerable distortion of the mercury and oxygen valency angles, as shown roughly above, would be required in any ring structure. A structure (II), besides being stereochemically unlikely

* From the principles laid down and the approximate values contained in the paper by Coop and Sutton (*loc. cit.*) we might expect that the two C=O bonds would give rise to about 10 c.c. of atom polarisation, the Hg–O bonds to about 7 c.c., and the remaining polar bonds to about 3 c.c., making *ca.* 20 c.c. in all and giving $\mu = 2{\cdot}65$ D.

because it has four-membered rings, is symmetrical, and hence incompatible with the observed dipole moment. An " open " structure (III) is thus left as the most likely one. The O–Hg–Hg–O system is supposed to be linear, in conformity with the linear configuration of mercuric compounds and of the crystalline mercurous halides.

On the assumptions (*a*) that, as in the esters (Marsden and Sutton, J., 1936, 1383), the O–Hg–Hg–O line is fixed *cis* with respect to the carboxyl groups, (*b*) that there is free rotation about the Hg–O bonds, (*c*) that the vector model (IV) is correct, it follows that the resultant moment of each rotating group is 1·34 D. directed

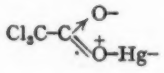
(III.) 

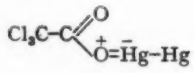


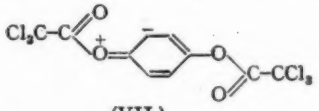
(IV.)

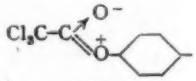
at about 12·5° above the C=O axis : the resolved components perpendicular to the O–Hg–Hg–O axis are each 1·20 D., whence the total moment should be 1·74 D. (*cf. Ann. Reports*, 1940, **37**, 59).

The effect of resonance with such structures as (V) would be markedly to increase this moment, and it is not inconceivable that the predicted value of the moment might rise to the observed value of 2·65 D. Since mercurous ion does not form complexes (*cf.* Latimer and Hildebrand, *op. cit.*) it seems unlikely that the structures (VI) need be considered.

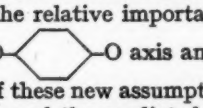
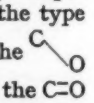

(V.)


(VI.)


(VII.)


(VIII.)

If the open structure (III) is correct, it should be analogous to that of *quinol bistrichloroacetate*, in which again there are two trichloroacetyl radicals bound to oxygens on the end of a linear system. The analogy is imperfect because of the conjugating power of the benzene nucleus. This compound was, however, prepared and its electric polarisation observed to be: $P_2 = 143 \pm 1$, $_EP_2 = 79{\cdot}0 \pm 0{\cdot}5$, whence $P_{A+O} = 64$ c.c. If P_A is 4 c.c., $\mu = 1{\cdot}70$ D.; and if P_A is 24 c.c., $\mu = 1{\cdot}32$ D.; so the best value seems to be $1{\cdot}50 \pm 0{\cdot}20$ D.

It is difficult to estimate the influence of the benzene nucleus on the moment; it seems that the principal effect of resonance of the type (VII) would be to decrease the relative importance of structures of the type (VIII), and thus to prevent freedom of rotation about the  axis and to allow it about the  axis. On the basis of the same vector model as before, and of these new assumptions, the resultant of the C=O and the CCl_3 moments perpendicular to the C–O axis is 0·87, and the predicted value of the total moment is 1·23. This is less than the observed value of 1·5, as would be expected since the assumptions represent an extreme state of affairs though the difference is the opposite of that between the calculated and the observed value of the moment of quinol diacetate, *viz.*, 3·3 and 2·2 D. We may, at least, safely say that the low moment of quinol bistrichloroacetate is *not* evidence *against* the open structure for mercurous trichloroacetate.

It is difficult to understand why mercurous trichloro- and trifluoro-acetate should be soluble in benzene, whereas mercurous acetate is not. One would expect a greater tendency for covalent bond formation between the mercury atom and the oxygen atom of the *weaker* acid. It is not difficult to understand why, of all common non-polar solvents, *only* benzene is effective as a solvent for these compounds; the greater solvating power and polarisability of benzene as a solvent are common experience, although little explicit recognition of this fact has been made in the literature (cf. Bloom and Sutton, J., 1941, 733).

Swarts (*Bull. Soc. chim. Belg.*, 1923, **32**, 111) observed that silver trifluoroacetate is soluble in benzene, and is polymerised at least to a dimer. We have observed that silver trichloroacetate is somewhat soluble in benzene, but the solution readily deposits silver chloride, so the matter was not studied further.

From the observed refractivity of mercurous trichloroacetate, and the calculated refractivity of the trichloroacetate group, the refractivity of mercurous mercury is calculated to be 13·2 c.c. The accepted value for mercuric mercury is 13·0 c.c., and this coincidence supports the belief that the electronic structures of the two are identical.

Experimental.

Preparation and Purification of Materials.—Benzene was purified as described by Hampson, Farmer, and Sutton (*Proc. Roy. Soc.*, 1933, *A*, **143**, 147).

Mercurous trichloroacetate was prepared by addition of a freshly prepared solution of mercurous nitrate to an aqueous solution of trichloroacetic acid (Bateman and Conrad, *loc. cit.*). The precipitate of very small white crystals, after drying, was never completely soluble in benzene, so it was purified by dissolution in benzene, filtering the solution, and precipitating it with ligroin (b. p. 40—60°) from which olefinic impurities had been removed with sulphuric acid (when

untreated ligroin was used, the precipitate gave low analytical results for mercury and chlorine and liberated a distinct odour of ligroin when dissolved in water) (Found : C, 6·6; H, 0·064; Cl, 28·9. Calc. for $Hg_2C_4O_4Cl_4$: C, 6·6; Cl, 29·3%).

Two methods were used to prepare *quinol bistrichloroacetate*. (1) Quinol was fused with a slight excess of trichloroacetic acid, about 2 c.c. of phosphorus oxychloride being added per g. of quinol. The mixture was kept at 110° for several hours, with stirring, until hydrogen chloride ceased to be evolved. The excess of phosphorus oxychloride was then carefully decomposed with water (cooling in ice-water). The resulting white powder was collected, washed with water, dried, and recrystallised from ligroin (b. p. 60—80°). This is a modification of Dzierzgowski's procedure for the monochloroacetate (*Ber.*, 1893, **26**, Ref. bd., p. 590). (2) Quinol and trichloroacetyl chloride were allowed to react in pyridine solution; the brown solid formed was collected and recrystallised from ligroin. The yield in either reaction was only about 15%; m. p. 136—136·5° (Found : C, 29·6; H, 1·05; Cl, 53·2. $C_{10}H_4O_4Cl_6$ requires C, 29·9; H, 1·0; Cl, 53·1%).

Stannic chloride does not cause reaction between trichloroacetyl chloride and quinol, although it causes an extremely vigorous reaction between acetyl chloride and quinol. Dimethylaniline also was not effective as a condensing agent for the former reaction.

Cryoscopic Measurements.—The molecular weight of mercurous trichloroacetate was determined in a Beckmann apparatus [$Hg_2(O_2C_2Cl_3)_2$ requires M, 726] :

Solute, g.	0·205	0·439	0·640	0·625	0·465
Solvent, g.	11·17	11·17	11·17	13·16	14·75
ΔT	0·125°	0·286°	0·408°	0·352°	0·234°
M	773	723	726	715	714

Electric Polarisation Measurements.—These were made with the apparatus described by Hampson, Farmer, and Sutton (*loc. cit.*) :

Mercurous trichloroacetate.

f_2.	ϵ.	d.	$d\epsilon/df_2$.	dd/df_2.	P_2.	n^2.	$_EP_2$.
0	2·2727	0·8733	—	—	—	2·2571	—
0·003124	2·3133	0·8930	13·00	6·328	245·7	2·2631	81·7
0·005545	2·3448	0·9084	13·00	6·316	245·0	2·2667	78·3
0·006109	2·3528	0·9118	13·11	6·297	248·3	2·2678	79·4
* 0·004106	2·3277	0·8989	—	—	244·3	2·2676	83·0

$\infty P_2 = 245{\cdot}7 \pm 1$ c.c.; $_EP_2 = 79{\cdot}5 \pm 2$ c.c.; $P_{A+O} = 166 \pm 3$ c.c.

Quinol bistrichloroacetate.

0	2·2727	0·8734	—	—	—	2·2571	—
0·007627	2·3084	0·8887	4·681	2·0152	144·0	2·2397	78·9
0·01509	2·3404	0·9032	4·487	1·9775	142·3	2·2622	79·2

$\infty P_2 = 143 \pm 1$ c.c.; $_EP_2 = 79{\cdot}0$ c.c.; $P_{A+O} = 64 \pm 1$ c.c.

* These data are for the sample used for analysis and for the first molecular-weight determination; this dissolved in benzene to leave a slight milky precipitate, presumably mercurous chloride. The agreement with the other data is satisfactory.

The authors thank Prof. N. V. Sidgwick, F.R.S., for his interest and advice, and Imperial Chemical Industries, Ltd., for a grant towards the cost of this research.

THE DYSON PERRINS LABORATORY AND THE PHYSICAL CHEMISTRY LABORATORY, OXFORD.

[*Received, June 27th*, 1942].

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112. *The Determination of the Angle between the Phenyl Groups in αα-Diphenylethylene, from Electric Dipole Moment Measurements.*

By G. E. COATES and L. E. SUTTON.

From the electric dipole moments obtained for αα-diphenylethylene and several *p*-substituted derivatives thereof, the valency angle between the attached phenyl groups has been calculated by methods previously developed. The value obtained is 125° ± 3°.

This large value can hardly be explained except by "resonance" involving the two benzene rings and the ethylenic double bond, which would make the two rings tend to be coplanar and so, by creating steric repulsion, cause the angle between them to be greater than that found in diphenylmethane (115° ± 5°) or for the CH_2 angle in ethylene (118°). It therefore confirms a conclusion reached by other workers from measurements of bond distances in other phenylethylenes.

The valency angle observed is not large enough to allow of the rings being coplanar, and in order to give the distance of 2·4 A. believed to be the minimum permissible between unbonded hydrogen atoms it is necessary that the rings be twisted about 30° out of the common plane.

THE method of determining the valency angle of the linking atom in diphenyl compounds by means of dipole moment measurements is now well established, and, in particular, methods have been developed by which the errors common in earlier work have been overcome (Hampson and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **140**, 562; Bennett, *Trans. Faraday Soc.*, 1934, **30**, 853; Sutton and Hampson, *ibid.*, 1935, **31**, 945; Coop and Sutton, J., 1938, 1869). The investigation of the angle in αα-diphenylethylene is of interest in connexion with the effect of resonance on the nature of carbon–carbon bonds in conjugated systems.

EXPERIMENTAL.

Preparation and Purification of Materials.—αα-Diphenylethylene. This was prepared by removal of the elements of water from diphenylmethylcarbinol (*Organic Syntheses*, **6**, 32). Special care was taken to ensure the absence of carbinol

from the product, which was purified according to Anschütz (*Annalen*, 1886, **235**, 336), and fractionated three times in a vacuum in an all-glass apparatus. A final distillation was carried out just before the dipole moment was measured; b. p. 145—146° (corr.)/14 mm. [Klages and Heilmann, *Ber.*, 1904, **37**, 1449, give b. p. 147° (corr.)/16 mm.].

α-Phenyl-α-p-chlorophenylethylene. This, and the other derivatives, were prepared by dehydration of the carbinol formed by hydrolysis of the reaction product from methylmagnesium iodide and the corresponding derivative of benzophenone. The preparation of the *p*-chloro-derivative is described by Bergmann and Bondi (*Ber.*, 1931, **64**, 1468). The compound had b. p. 157° (corr.)/12 mm. (four distillations in a vacuum).

α-Phenyl-α-p-bromophenylethylene. After five vacuum distillations, this compound boiled at 185° (corr.)/10 mm. Stoermer and Simon (*Ber.*, 1904, **37**, 4168) described the substance as an oil, b. p. 199—201°/19 mm., but it was possible to crystallise it from ethyl alcohol by cooling the solution in ice–salt, and after four crystallisations it was obtained as white crystals, m. p. 25·5—26·0° (corr.).

αα-Di-p-chlorophenylethylene. This was prepared from *pp'*-dichlorobenzophenone as described by Bergmann and Bondi (*loc. cit.*), who gave m. p. 91°. After three crystallisations from methyl alcohol–benzene (7 : 1 by vol.), the m. p. became constant at 86·2—86·5° (corr.), unchanged after a crystallisation from purified light petroleum and after six crystallisations from methyl alcohol (Found: C, 67·2; H, 4·1. Calc. for $C_{14}H_{10}Cl_2$: C, 67·5; H, 4·1%).

αα-Di-p-bromophenylethylene. Prepared from *pp'*-dibromobenzophenone, this *substance* had m. p. 85·8—86·2 (corr.) (Found: C, 49·9; H, 3·0. $C_{14}H_{10}Br_2$ requires C, 49·7; H, 3·0%), depressed by 8—9° on admixture with di-*p*-chlorophenylethylene; it is slightly soluble in boiling methyl alcohol and very sparingly soluble in cold; it is very much more soluble in ethyl alcohol, benzene, and acetic acid. The solubility in light petroleum is very small.

αα-Di-p-fluorophenylethylene. When the diazonium borofluoride from *pp'*-diaminodiphenylmethane was heated, it afforded pp'-*difluorodiphenylmethane*, m. p. 27·0—27·4°, b. p. 263·5° (corr.)/754 mm. (Found: C, 76·2; H, 5·0. $C_{13}H_{10}F_2$ requires C, 76·5; H, 5·0%); this is easily soluble in all the usual organic solvents and has a characteristic smell similar to but a little sweeter than that of diphenylmethane. Oxidation with chromic acid gave the corresponding benzophenone, from which *αα-di-p-fluorophenylethylene* was prepared in the usual way. After four distillations in a vacuum the b. p. was 137·5—138·5° (corr.)/12 mm., and after four crystallisations from ethyl alcohol the m. p. was 46·5—47·0° (corr.) (Found: C, 77·7; H, 4·9. $C_{14}H_{10}F_2$ requires C, 77·8; H, 4·6%). The compound crystallises from ethyl alcohol in short thick prisms, and is easily soluble in all the usual solvents except cold ethyl alcohol and cold light petroleum.

Benzene. Benzene was the solvent used for all measurements, special precautions being taken to ensure dryness (see Hampson and Sutton, *loc. cit.*).

Measurement of Dipole Moments.—The dielectric constant, refractive index, and density of dilute benzene solutions were measured at 25° by means of the apparatus and procedure described by Sutton (*Proc. Roy. Soc.*, 1931, *A*, **133**, 668). The refractivities were measured at the frequency of the mercury line λ 5461 A. Auwers and Eisenlöhr (*J. pr. Chem.*, 1911, **84**, 49) measured the refractivity of *αα*-diphenylethylene at various frequencies in the visible region, and extrapolation to zero frequency indicates that the electron polarisation at 5461 A. exceeds that at zero frequency by 2—2·5 c.c. It was assumed that the same frequency variation occurred in the substituted compounds measured. The measured refractivities agreed well with those calculated from tables, if the same allowance for optical exaltation was made as was observed from *αα*-diphenylethylene.

The methods available for determination of atom polarisation, *viz.*, determination of refractive index in the far infra-red and well away from absorption bands, plotting total polarisation against $1/T$ and measuring from the graph the polarisation at $1/T = 0$, and determination of the dielectric constant of the solid substance, all in effect involve the atom polarisation as the small difference between two large numbers, and are experimentally difficult. The method adopted here was to take the atom polarisation of one compound (α-phenyl-α-*p*-chlorophenylethylene) to be 3 c.c., *i.e.*, approximately 5% of P_E (cf. Groves and Sugden, J., 1935, 971), and to make the values for the other compounds proportional to 3 c.c. according as their moments compare with that of α-phenyl-α-*p*-chlorophenylethylene, a procedure in general accordance with modern ideas about atom polarisation. The atom polarisations calculated in this way did not differ much from 3 c.c. It is most unlikely that the true values differ from 3 c.c. by more than ± 2 c.c., and this difference would cause a variation of calculated angle of only ± 1—1·5°.

Experimental Results.—The dipole moment data are given in the table, in which P represents the total polarisation, P_E the electron polarisation, P_A the atom polarisation, and μ the dipole moment in Debye units.

Compound.	P.	P_E.	P_A.	μ.
αα-Diphenylethylene	62·1	59·1 †	(see below)	0·0—0·38 ‡
α-Phenyl-α-*p*-chlorophenylethylene	113·6	64·1 †	3·0	1·49
αα-Di-*p*-chlorophenylethylene	115·0	69·3,† 69·0 *	3·3	1·43 §
α-Phenyl-α-*p*-bromophenylethylene	117·0	67·6,† 66·6 *	2·9	1·50
αα-Di-*p*-bromophenylethylene	120·9	74·8 *	3·3	1·43
αα-Di-*p*-fluorophenylethylene	110·0	59·1 *	3·1	1·52

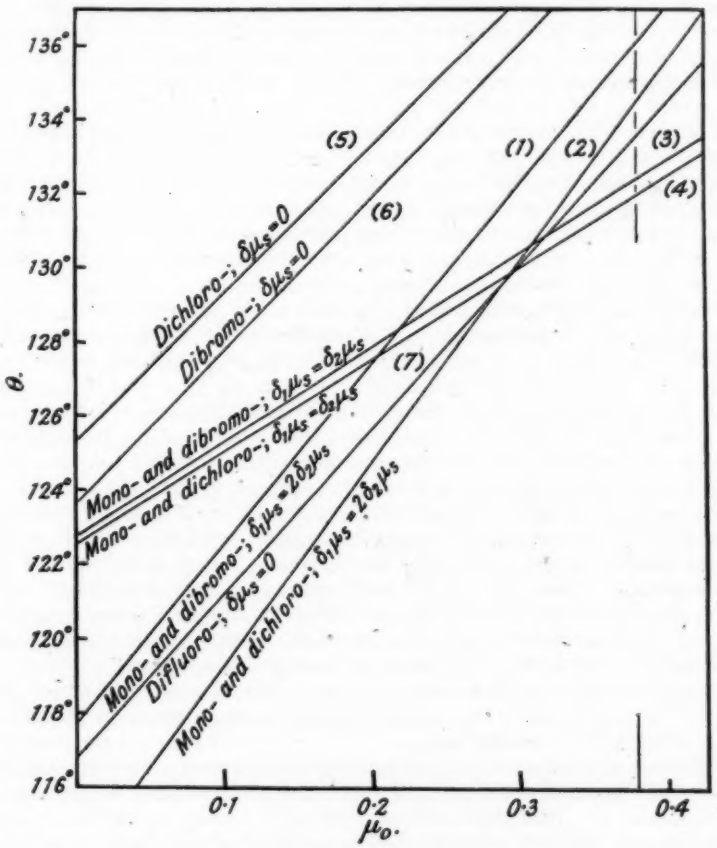
* From refractivity tables. † From observed refractivities.
‡ Smyth and Dornte (*J. Amer. Chem. Soc.*, 1931, **53**, 1296) give $\mu = 0{\cdot}58$ D. at 70°, 0·35 D. at 10°.
§ Bergmann, Engel, and Meyer (*Ber.*, 1932, **65**, 446) give $\mu = 1{\cdot}39$ D.

Until the atom polarisation of *αα*-diphenylethylene is evaluated, we can only say that the moment, μ_0, of the substance lies between 0 and 0·38 D., and we shall take these as the initial limits.

The values of the valency angle, θ, of the quaternary linking carbon atom were calculated according to the method described by Hampson and Sutton (*loc. cit.*), whereby allowance is made for interaction of the $>C{=}CH_2$ and substituent groups, for values of the moment of *αα*-diphenylethylene over the above range. Two sets of corrected values for the valency angle were obtained, one based on the assumption that the interaction in each substituted ring is the same in the mono- as it is in the di-substituted compound ($\delta_1\mu_S = \delta_2\mu_S$), and the other on the assumption that the interaction in the former is twice that in the latter ($\delta_1\mu_S = 2\delta_2\mu_S$), these being the extremes between which the true state of affairs probably lies. The relevant values for the moments of halogenated benzenes, μ_S, were obtained from the measurements in benzene solution recorded in " A Table of Dipole Moments " (*Trans. Faraday Soc.*, 1934, **30**, Appendix), *viz.*, fluorobenzene, 1·45; chlorobenzene, 1·56; bromobenzene, 1·52 D. None of the moments is corrected for solvent effect; but in this particular application solvent effect produces only a minor error (Coop and Sutton, J., 1938, 1869).

In the figure these values of θ are plotted as a function of μ_0 (curves 1—4). Some derived from the disubstituted compounds without any correction for interaction are also shown (curves 5 and 6). It will be seen that the above limits of μ_0 give the extreme limits for the angle θ as 114—136°—more probable limits being *ca.* 120—134°. The atom polarisation is certainly not zero, however, so μ_0 must be less than 0·38 and the real upper limit for θ must be lower. Sugden (*Trans. Faraday Soc.*, 1934, **30**, 734) reports $P_A = 1{\cdot}7$ c.c. for triphenylmethane, so that P_A for *αα*-diphenylethylene is probably not less than 1·1 c.c., corresponding to $\mu_0 = 0{\cdot}30$ D. and $\theta > 131°$. The sum of twice the atom polarisability

for benzene (1·1 c.c.; Groves and Sugden, J., 1934, 1097) and for ethylene (0·39 c.c.; Watson and Ramaswamy, *Proc. Roy. Soc.*, 1936, *A*, **156**, 144) is 2·6 c.c. If the source of the atom polarisation is the effect of the field on the slightly polar bonds, additivity would be expected (Audsley and Goss, J., 1941, 864). This would correspond to a value of 0·14 D. for μ_0 and an upper limit of 126·5° for θ. From unpublished work in this Laboratory by Mr. N. J. Leonard, and from the fact that the electric polarisations of aromatic compounds are unaltered by the substitution of hydrogen by fluorine, it appears that the interaction moments in *p*-substituted fluoro-compounds are small or zero; θ values have therefore been calculated from the moment of αα-di-*p*-fluorophenylethylene without any correction for interaction. They are shown by curve 7 which obviously is quite different from curves 5 and 6 and agrees well with curves 1 and 2. It will be noticed, however, that the two curves for the values derived from the chloro- and bromo-compounds agree much better when it is assumed that $\delta_1\mu_s = \delta_2\mu_s$ (curves 3 and 4) than when it is assumed that $\delta_1\mu_s = 2\delta_2\mu_s$ (curves 1 and 2). It may therefore be concluded that more weight can be attached to the former two curves than to the others, so the lower limit for θ now appears to be *ca.* 122°. The true value of the angle therefore probably lies between 122° and 128°. There is little point in trying to fix closer limits from the available data.



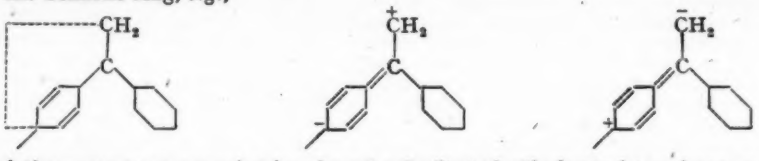
Discussion.

The valency angle of the quaternary carbon atom linking the two phenyl groups in αα-diphenylethylene was found to be 125° ± 3°; this is an unusually large value for an angle between single carbon valencies. The valency angles of the linking carbon atoms in diphenyl compounds are probably decided by the following three factors: (1) The natural valency angle of the atom for its particular valency state. (2) Repulsion between hydrogen atoms in the *o*-positions of the benzene rings. (3) Resonance leading to partial double-bond formation between the linking atom and the benzene rings; this promotes a coplanar configuration in which effect (2) is very strong, causing a widening of the angle.

The angle between the phenyl groups in *p*-substituted diphenylmethane has been found from electric dipole moment measurements to be 115° ± 5° (Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **143**, 147). This is rather larger than the tetrahedral angle, 109·5°, but a slight increase in the angle may be expected from the operation of effect (2), which should be increased by thermal agitation. In this connection, measurements on diphenylmethane derivatives at high temperatures would be of interest.

In αα-diphenylethylene the linking carbon atom is part of a group containing a double bond $CH_2{=}C<$ and is in the trigonal sp^2 state, in which the natural valency angle is 120° (Penney, "The Quantum Theory of Valency," Methuen, 1935, Chap. IV)—compare the CH_2 angle of 118° in ethylene (Badger, *Physical Rev.*, 1934, **45**, 648; Penney, *Proc. Roy. Soc.*, 1937, *A*, **158**, 317). The observed angle is some 5° or more greater than the natural angle; this suggests that effects (2) and (3) are operative. Resonance leading to the formation

of partial double bonds between the linking atom and the benzene rings is to be expected, because many Lewis–Langmuir structures can be drawn for the substance, in which there is a double bond between the quaternary carbon atom and the benzene ring, *e.g.*,



Calculations of the resonance energies in phenyl-substituted ethylenes have been made by Pauling and Sherman (*J. Chem. Physics*, **1933**, **1**, 679) and by Wheland (*ibid.*, **1934**, **2**, 474). The heats of formation derived from heats of combustion are consistent with the results of these calculations; but, in direct conflict with theory, the heat of hydrogenation of styrene (Dolliver, Gresham, Kistiakowsky, and Vaughan, *J. Amer. Chem. Soc.*, **1937**, **59**, 831) indicates almost no resonance at all. The available thermal evidence must therefore be considered inconclusive for the purpose of showing whether resonance of this type is important in these compounds.

Calculations of its effects on the length of the carbon–phenyl bond in styrene and stilbene have been made by Penney and Kynch (*Proc. Roy. Soc.*, **1938**, *A*, **164**, 409), also by Lennard-Jones and Coulson (*Trans. Faraday Soc.*, **1939**, **35**, 811); and these agree exactly with the values found experimentally by Robertson and Woodward (*Proc. Roy. Soc.*, **1937**, *A*, **162**, 568), who found, from *X*-ray analysis of the stilbene crystal, a length of 1·44 A., corresponding to a bond order [on the Penney length/order scale (*loc. cit.*)] of 1·31. These facts are in harmony with the conclusions from our results, *viz.*, that conjugation between the benzene rings and the ethylenic double bond occurs to a very marked degree.

If there were the maximum possible degree of double-bonding between the linking carbon atom and the phenyl groups, the two latter should be coplanar. The van der Waals radius of hydrogen being taken as 1·2 A. (Pauling, "The Nature of the Chemical Bond," Cornell, 1940, p. 189) and the interatomic distances (Pauling, *op. cit.*, pp. 168, 172, 218) as: $C_{ar.}$–H = 1·09, $C_{ar.}$–$C_{ar.}$ = 1·39, $C_{ar.}$–$C_{qu.}$ = 1·45 A., it can easily be shown that for the phenyl groups to be coplanar with the ortho-hydrogen atom nuclei 2·4 A. apart, the angle between them must be 160°. Now, according to our calculations, the upper limit for this angle must be about 130°, and if the phenyl groups were coplanar the H–H internuclear distance would then be only 1·08 A. It is therefore probable that the phenyl groups are twisted out of a common plane. If θ is 130° the angle of twist, ψ, must be 28°; if θ is 125°, ψ must be 29·5°; and if θ is 120°, ψ must be 31°; so, to make the H–H distance the 2·4 A. which is believed to be necessary, the phenyl groups must be twisted about 30° out of the common plane.

A similar twisting is observed in *cis*-azobenzene (Robertson, J., 1939, 232) where it is as much as 50° and results in a notable diminution of the conjugation of the phenyl groups with the $-N{=}N-$ group as shown by the increase in length of the Ph–N= bonds. From the dimensions supplied by the author and some of the bond lengths previously quoted, it is easy to calculate that the H–H distance in this configuration is 2·26 A., which is very close to what has been taken above as the distance of minimum approach.

The final configuration may be regarded as attained through the contest between the steric repulsion of the hydrogen atoms and the resistance of the valency angle to enlargement, on the one hand, and resonance in favouring a coplanar configuration, on the other.

This work adds to the already large body of evidence that resonance can have marked effects upon spatial configurations of molecules. The converse has also been demonstrated by Birtles and Hampson (J., 1937, 10) and Ingham and Hampson (J., 1939, 981), who showed that spatial configuration affects resonance. The reality of a connection between the two can therefore be taken as established.

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THE DYSON PERRINS LABORATORY AND THE PHYSICAL CHEMISTRY LABORATORY, OXFORD.

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113. *Potassium Alkaneselenonates and Other Alkyl Derivatives of Selenium.*

By MARJORIE L. BIRD and FREDERICK CHALLENGER.

Methane-, ethane-, and propane-1-seleninic acids give the potassium salts of the corresponding alkaneselenonic acids, $R{\cdot}SeO_3H$, on oxidation with potassium permanganate. These eliminate selenious acid on treatment with hot dilute acid. Methaneselenonic acid is also formed on oxidation of dimethyl selenide with the same reagent. Alkaneseleninic acids, $R{\cdot}SeO_2H$, are formed on oxidation of dimethyl selenide with hydrogen peroxide or by the action of aqueous silver oxide on diethyl and di-*n*-propyl selenide dibromides. The dihydroxide or selenoxide, $(CH_3)_2Se(OH)_2$ or $(CH_3)_2SeO$, is formed from dimethyl selenide by the action of concentrated hydrogen peroxide or of aqueous silver oxide on the dibromide. Dialkyl diselenides can be converted into methyl alkyl selenides by reduction with sodium and alcohol and treatment with methyl iodide. Dialkyl diselenides undergo fission with mercuric salts.

SOME of the alkylated derivatives of selenium described in this communication were prepared with a view to a study of their behaviour in bread cultures of certain moulds, particularly *Scopulariopsis brevicaulis* (see follow-

ing paper). Others were prepared in order to facilitate the identification of products of mould metabolism, or of the oxidation of the dialkyl selenides.

The method of Tschugaeff and Chlopin (*J. Russ. Phys. Chem. Soc.*, 1915, **47**, 364) for the preparation of alkyl selenides and tellurides (see Balfe, Chaplin, and Phillips, J., 1938, 341; Balfe and Nandi, J., 1941, 70) can also be employed in the case of diselenides, an extra atomic proportion of selenium being used.

The following crystalline derivatives of the dialkyl monoselenides (Me, Et, and *n*-Pr) have been prepared: *dimethylselenetine bromide*, $Me_2Se(Br)\cdot CH_2\cdot CO_2Et$, *diethyl selenide dibromide* (previously described as an oil), and di-*n*-propyl selenide dibromide.

Dialkylselenones have not been described, although methyl- and ethyl-β-naphthylselenones have been obtained by Loevenich, Fremdling, and Föhr (*Ber.*, 1929, **62**, 2856). The action of hydrogen peroxide on dimethyl selenide gave no selenone but either methaneseleninic acid (with loss of a methyl group) or a mixture of this acid with dimethyl selenide dihydroxide, $(CH_3)_2Se(OH)_2$, or dimethyl selenoxide, $(CH_3)_2SeO$. The mixture was identified by its behaviour with hydrobromic acid, giving methylselenium tribromide and dimethyl selenide. Similar results were obtained in the tellurium series by Balfe, Chaplin, and Phillips (*loc. cit.*), who state that *n*-butyl telluride on oxidation with air or neutral hydrogen peroxide gives double compounds of di-*n*-butyl telluroxide and *n*-butyltellurinic acid, *e.g.*, $2TeBu_2O,BuTeO\cdot OH$, and also butyric acid. They regard the last two compounds as oxidation products of *n*-butyltellurol and *n*-butaldehyde arising thus: $(C_4H_9)_2TeO = C_3H_7\cdot CHO + C_4H_9\cdot TeH$. They also draw attention to similar decompositions of alkyl selenoxides and sulphoxides (see also Challenger and Rawlings, J., 1937, 870).

This formation of the dihydroxide or selenoxide suggested an examination of the action of aqueous silver oxide on R_2SeBr_2. The diethyl and di-*n*-propyl dibromides gave the slightly impure silver salts of ethaneseleninic acid and propane-1-seleninic acid. The dimethyl derivative gave the dihydroxide or selenoxide, identified as before, and a trace of an acidic product, probably the seleninic acid. The product altered in m. p. on keeping in a desiccator and may then have contained complex compounds analogous to the tellurium derivatives described by Balfe and his co-workers (*loc. cit.*). On heating, both specimens decomposed, giving formaldehyde, presumably thus: $(CH_3)_2SeO = CH_2O + CH_3\cdot SeH$ (see above). Formaldehyde is also produced on heating methaneseleninic acid, the reaction probably proceeding thus:

$$2CH_3\cdot SeO_2H = CH_2O + CH_3\cdot SeH + H_2O + SeO_2.$$

When methane-, ethane-, and propane-1-seleninic acids or their hydrogen nitrates are carefully oxidised with potassium permanganate in almost neutral solution, the potassium salts of the alkaneselenonic acids are obtained. Alkaneselenonic acids have not previously been described, although certain aromatic analogues have been prepared by a similar method (Pyman, J., 1919, **115**, 166) and also by the action of selenic acid on aromatic hydrocarbons (Doughty, *Amer. Chem. J.*, 1909, **41**, 326; Anschütz, Kallen, and Riepenkröger, *Ber.*, 1919, **52**, 1860; Anschütz and Teutenberg, *Ber.*, 1924, **57**, 1018). The salts of the alkaneselenonic acids readily eliminate selenious acid on heating with dilute acid or alkali. Like their aromatic analogues they explode slightly on heating. Potassium ethaneselenonate is gradually decomposed by warm aqueous permanganate, evolving some acetaldehyde; the methyl derivative is stable under these conditions.

Mr. J. W. Fletcher (private communication) found that, on oxidation with permanganate, dimethyl selenide yields methaneseleninic acid, methaneselenonic acid and selenious acid. These were isolated as the free acid, the potassium and the barium salt respectively and analysed.

The conversion of diselenides into selenothiols on reductive fission with sodium and alcohol was employed in the preparation of methyl ethyl and methyl *n*-propyl selenides. These were conveniently obtained by direct treatment of the alkaline solution of the selenothiol with the required alkyl halides. They were characterised as the mercurichlorides.

The dialkyl disulphides undergo fission with mercuric chloride, yielding, in the first instance, R·S·HgCl and R·SCl, but are stable to mercuric cyanide (Challenger and Rawlings, J., 1937, 868). Both these mercuric salts, however, cause fission of the dialkyl diselenides. The products have not been so carefully examined as in the case of the disulphides, but with dimethyl and diethyl diselenides an alkyl selenocyanate is formed; the other products appear to be cyanomercurymethylselenothiol, $CH_3\cdot Se\cdot HgCN$, and dimercury ethylselenothiol $(C_2H_5\cdot Se)_2Hg$.

With dimethyl diselenide and mercuric chloride the insoluble product appears to be a mixture of $CH_3\cdot Se\cdot HgCl,HgCl_2$ with a little $CH_3\cdot Se\cdot HgCl$ (compare Challenger and Rawlings, *loc. cit.*). The aromatic diselenides also undergo fission with bromine, giving arylselenium bromide, R·SeBr, and tribromide, $R\cdot SeBr_3$ (Behaghel and Seibert, *Ber.*, 1932, **65**, 812).

Although selenious acid does not appear to give rise to compounds derived from the form $H\cdot SeO_2H$ (Strecker and Daniels, *Annalen*, 1928, **462**, 186), β-naphthaleneseleninic acid gives both seleninic esters and selenones according to the particular reagent employed (Loevenich, Fremdling, and Föhr, *Ber.*, 1929, **62**, 2856). Neither ester nor selenone is produced from sodium methaneseleninate and methyl sulphate or from the sodium or silver salt with methyl iodide. Iodine is liberated in the latter case, probably thus: (*a*) $CH_3\cdot SeO_2Na + CH_3I + HOH = CH_3\cdot SeO_2H + NaI + CH_3\cdot OH$; (*b*) $2CH_3\cdot SeO_2H + 6NaI + 2H_2O = (CH_3)_2Se_2 + 6NaOH + 3I_2$.

Experimental.

Preparation of Alkyl Selenides.—A mixture of sodium formaldehydesulphoxylate ("rongalite") (90 g.; 0·76 mol.), sodium hydroxide (70 g.; 1·75 mols.), powdered selenium (25 g.; 0·32 mol.), and water (300 c.c.) was warmed to about

50° and slowly treated with the alkyl iodide (Me = 41·5 c.c., Et = 54 c.c., and *n*-Pr = 67·5 c.c.; 0·32 mol. in each case). The reaction was vigorous with methyl iodide and in all cases was completed by warming under reflux for 1—3 hours. If addition of the methyl and ethyl iodides was too rapid, the yield of selenide was diminished owing to the formation of the trialkylselenonium iodide, which separated on the sides of the flask. Dimethyl selenide was removed on the water-bath; the homologues were separated on addition of water and extraction with ligroin. Distillation yielded pure products having the b. p. given in the literature. The yields of the methyl and *n*-propyl selenides were 88 and 54%. That of the ethyl compound was of the same order. The method is a very convenient one.

Dimethylselenetine bromide was prepared from dimethyl selenide and ethyl bromoacetate and after crystallisation from alcohol–ether melted at 90° (decomp.) (Found: Br, 29·0. $C_6H_{13}O_2BrSe$ requires Br, 29·0%).

Diethyl selenide dibromide was obtained from the selenide and the calculated amount of bromine, both in cooled carbon tetrachloride. The solvent was removed under diminished pressure, and the residue cooled, giving brown plates, in theoretical yield, m. p. 37° (decomp.). They were not recrystallised (Found: Br, 54·0. Calc. for $C_4H_{10}Br_2Se$: Br, 53·9%). This compound is stated to be an oil. After 6 months in a closed tube decomposition to black selenium, m. p. 217°, had occurred.

Di-n-propyl selenide dibromide. The selenide (0·1 mol.) and bromine (0·2 mol.) in carbon tetrachloride gave a red oil which soon solidified to orange crystals, m. p. 50°; yield, theoretical. They were recrystallised from hot dilute hydrobromic acid (Found: Br, 49·1. $C_6H_{14}Br_2Se$ requires Br, 49·2%). The dibromide is insoluble in cold water but soluble in hot, giving a colourless solution. It is very soluble in ether, alcohol, and acetone. After 6 months in a closed tube it had almost completely decomposed to black selenium, m. p. 217°, and a red liquid smelling like *n*-propyl bromide.

Oxidation of Dimethyl Selenide with Hydrogen Peroxide.—"Perhydrol" and the cooled selenide were not miscible, but on standing the temperature rose and a vigorous reaction occurred, giving a homogeneous solution. After being heated at 100° for 30 minutes, this was evaporated at 16 mm. The residue solidified in a desiccator overnight, giving white needles, m. p. 131°, unchanged on recrystallisation from chloroform (Found: C, 9·8; H, 3·2; equiv., by titration with NaOH, 128. Calc. for CH_4O_2Se: C, 9·5; H, 3·2%; equiv., 127. Calc. for CH_4O_3Se: C, 8·4; H, 2·8%). Its identification as methaneseleninic acid was confirmed by the production of an odour of methyl hydrogen selenide on reduction with zinc and hydrochloric acid, and by the formation of a salt with benzenesulphonic acid, m. p. 150° (decomp.); Backer and van Dam (*Rec. Trav. chim.*, 1935, **54**, 535) give m. p. 150° (decomp.). When the seleninic acid was gently warmed, formaldehyde was evolved; it was identified by its odour and by the formation of the 2 : 4-dinitrophenylhydrazone, m. p. 161°, and mixed m. p. 162—165° with an authentic specimen of m. p. 165°. A yellow oil, turning red and then volatilising, giving a residue of red selenium and a sublimate of white needles, probably selenium dioxide, was also produced. A concentrated aqueous solution of the seleninic acid gave with hydrobromic acid hygroscopic orange crystals, m. p. 75° (decomp.). These could not be recrystallised from water or hydrobromic acid and depressed the m. p. of dimethyl selenide dibromide (85°) to 65°. Titration showed them to be slightly impure *methylselenium tribromide* (Found: Br, 70·0. CH_3Br_3Se requires Br, 71·9%). The seleninic acid was also obtained from dimethyl selenide with perhydrol in glacial acetic acid. 90% Hydrogen peroxide being used without a solvent, crystals of methaneseleninic acid separated from the concentrated reaction mixture. Removal of these and treatment of the residue with hydrobromic acid gave (*a*) yellow needles, m. p. and mixed m. p. 86° (decomp.) with dimethyl selenide dibromide (m. p. 90° decomp.), and (*b*) methylselenium tribromide, m. p. 75° (decomp.).

Dimethyl Selenide Dibromide and Silver Oxide.—The dibromide was ground with water and a very slight excess of silver oxide. The clear neutral filtrate was evaporated at ordinary temperature under diminished pressure and left over sulphuric acid in a vacuum desiccator for 7 days; the very deliquescent residue (A) then solidified, m. p. 86° in a sealed tube. This gave formaldehyde on heating and was distinctly acid to litmus. With hydrobromic acid it regenerated the dibromide, m. p. and mixed m. p. 85°. On keeping over sulphuric acid for 3 months the m. p. of A rose to 135°, and 136° (decomp., giving formaldehyde and a red oil) on recrystallisation from alcohol. Mixed m. p. with methaneseleninic acid (m. p. 127°) was 105°. With hydrobromic acid the dibromide ($(CH_3)_2SeBr_2$ was regenerated. When the dibromide was treated with a large excess of silver oxide in water, and the alkaline filtrate shaken with norit and evaporated as before, neutral white crystals, m. p. 127°, containing neither silver nor halogen were obtained. These products were not further examined (see p. 571).

Diethyl Selenide Dibromide and Silver Oxide.—This reaction proceeds differently from that with the dimethyl derivative. Excess of aqueous silver oxide gave a silver salt on evaporation at 100°/15 mm., which appeared to be slightly impure silver ethaneseleninate (Found: equiv., 255. Calc. for $C_2H_5O_2AgSe$: equiv., 248). An ethyl group was therefore lost during the operation.

Di-n-propyl Selenide Dibromide and Silver Oxide.—Almost twice the amount of silver oxide necessary to remove all the bromine was required and the aqueous filtrate was evaporated at 50°/16 mm. A brownish powder separated which appeared to be slightly impure silver *n*-propaneseleninate (Found: equiv., 252. Calc. for $C_3H_7O_2AgSe$: equiv., 260). The aqueous filtrate had a sweet ester-like odour, possibly due to *n*-propyl propionate arising from the action of silver oxide on propaldehyde.

Oxidation of Alkaneseleninic Acids.—(a) *Potassium methaneselenonate.* Methaneseleninic acid (5·9 g.) and potassium hydroxide (0·83 g.; 0·015 mol.) were dissolved in water (15 c.c.) and slowly treated during 10 minutes with potassium permanganate (4·8 g.; 0·03 mol.) in water (90 c.c.). The quantities were calculated so that the solution should be almost neutral on completion of the oxidation. The mixture became warm and was finally exactly neutralised with potassium hydroxide and filtered. Evaporation under diminished pressure at about 40° (an essential precaution in all cases) left a white residue (6—7 g.), which was recrystallised from alcohol, giving shining white crystals. This and the other potassium salts of the selenonic acids were analysed by heating with hydrochloric acid under reflux for 3 hrs. (an alcohol is then eliminated, leaving selenious acid), diluting the solution with water, treating it with sulphur dioxide and hydrazine hydrate, and weighing the precipitated selenium (Found: Se, 43·3. CH_3O_3KSe requires Se, 43·6%). A similar decomposition occurs with hot baryta water, giving barium selenite. In the cold no trace of precipitate was obtained with baryta, indicating the absence of selenite and selenate. The absence of potassium alkaneseleninate was shown by the following comparative tests:

Reagent.	$CH_3{\cdot}SeO_2H$.	$CH_3{\cdot}SeO_3K$.
Warm hydrochloric acid	Decided odour of alkyl Se compound. No precipitate of Se.	Decomposition with effervescence. No odour. No precipitate of Se.
$NaHSO_3$	Yellow oil, odour of $CH_3{\cdot}SeH$. No Se.	No odour. No Se.
$NaHSO_3$ + HCl	As for $NaHSO_3$.	No odour. Se precipitated.
Zinc and acetic acid	Yellow oil, odour of $CH_3{\cdot}SeH$. No Se.	No odour. Se precipitated.

(b) *Potassium ethaneselenonate* was similarly prepared from ethaneseleninic acid (2·9 g.) and potassium hydroxide (0·38 g.), in water (8 c.c.), and potassium permanganate (2·15 g.) in water (45 c.c.). An odour of acetaldehyde was noticed towards the conclusion of the oxidation. The mixture was kept at room temperature for 2 hours and treated

as in (*a*). Crystallisation from alcohol containing a drop of water gave shining white plates free from selenite, selenate or ethaneseleninate (Found : Se, 40·0. $C_2H_5O_3KSe$ requires Se, 40·5%). The yield was not so good as in (*a*) owing to the more easy oxidation of the ethyl group (compare p. 572). Thus *potassium ethaneselenonate* is very sensitive to excess of potassium permanganate, whereas the corresponding methyl compound is stable to the warm reagent. The oxidation of ethaneseleninic acid hydrogen nitrate ($C_2H_5 \cdot SeO_2H,HNO_3$) with potassium permanganate and an extra equivalent of potassium hydroxide also gave pure potassium ethaneselenonate on extraction of the product with alcohol.

(c) *Potassium propane-1-selenonate* was similarly prepared from propane-1-seleninic acid hydrogen nitrate (12·1 g.), potassium hydroxide (4·15 g.) in water (30 c.c.) and potassium permanganate (5·8 g.) in water (120 c.c.). The salt formed shining white plates from alcohol, which were dried at 100°/15 mm. for 3 hrs. (Found : Se, 38·0. $C_3H_7O_3KSe$ requires Se, 37·6%). Selenate, selenite, and alkaneseleninate were absent. Yield, 40%.

As the potassium alkylselenonates were intended as substrates for the mould *Scopulariopsis brevicaulis*, it was essential to prove that they actually had the structure assigned to them, and that they were not, in fact, potassium alkyl selenates $RO \cdot SeO_2 \cdot OK$ or potassium alkyl selenites $RO \cdot SeO \cdot OK$. Their preparation from the diselenides through the seleninic acids seemed conclusive evidence on this point, but further confirmation was sought. The presence of a C–Se link in each compound was shown by the production of an intense odour of an alkylselenothiol on addition of aluminium amalgam to an aqueous solution of the salt. This reaction is also given by the corresponding potassium alkaneseleninates $R \cdot SeO_2K$. Their absence was, however, demonstrated by the sodium hydrogen sulphite test (see above), which gave no odour of a selenothiol. After 2 years the three potassium alkaneselenonates all gave a precipitate with barium hydroxide solution, which was soluble in dilute hydrochloric acid, indicating the presence of some selenite and consequent partial decomposition. This was only slight in the case of the methyl and the ethyl derivative and more pronounced with the propyl compound. Recrystallisation of the potassium propane-1-selenonate from alcohol removed the impurity and after 6 weeks in a closed tube the specimen was still free from selenite and also from seleninate, although a faint odour of an alkyl selenide or selenothiol could be detected on opening the tube.

Action of Methyl Iodide and of Methyl Sulphate on Salts of Methaneseleninic Acid.—The seleninic acid (7·6 g.) was exactly neutralised with sodium carbonate and evaporated at 50°/10 mm., giving a viscous residue which when kept in a vacuum desiccator over sulphuric acid gave long deliquescent needles of the sodium salt. These (8·9 g.; 0·06 mol.) were dissolved in hot alcohol, cooled, and treated with methyl iodide (8·5 g.; 0·072 mol.). No apparent reaction took place, so the mixture was heated for 4 hrs. at 100°; it then gradually darkened. Removal of solvent under diminished pressure left a residue with an unpleasant odour, containing free iodine. Removal of this with sodium thiosulphate left a dark oil with an odour of dimethyl diselenide.

Aqueous methaneseleninic acid was warmed with silver oxide, needles of the silver salt separating from the filtrate. These were left in methyl alcohol with a slight excess of methyl iodide for 20 hrs. Evaporation of the filtrate gave methaneseleninic acid, m. p. and mixed m. p. 134° (decomp.). The residue of silver iodide contained no selenium compound.

Methaneseleninic acid in excess of sodium hydroxide solution was shaken with the calculated quantity of methyl sulphate and left till the mixture was homogeneous. Extraction with chloroform removed nothing, before or after heating under reflux, though an unpleasant odour was noticed. Unchanged seleninic acid was recovered on evaporation with dilute nitric acid and extraction with ethyl acetate.

Preparation of Dialkyl Diselenides.—The methyl, ethyl, and *n*-propyl derivatives were very conveniently obtained by gradual addition of the calculated quantity of methyl sulphate, ethyl sulphate, and *n*-propyl iodide to a solution of two atomic proportions of selenium in the exact amounts of sodium hydroxide and sodium formaldehydesulphoxylate necessary to form sodium diselenide. Details are given for dimethyl diselenide. Selenium (32 g.) was completely dissolved in a mixture of sodium hydroxide (16 g.) and sodium formaldehydesulphoxylate (25 g.) in water (250 c.c.). Methyl sulphate (22 c.c.) was added and after heating for 1 hr. the reddish-brown colour had almost completely disappeared and a heavy oil separated. This was extracted with chloroform, dried over sodium sulphate, and fractionated, giving a little dimethyl selenide and 22 g. of the diselenide as an orange oil, b. p. 153°; yield, 60%. This was fractionated three times, the b. p. remaining constant at 153°/16 mm. Van Dam gives b. p. 155—157°/21 mm.

Diethyl diselenide was obtained in 60% yield and boiled constantly at 85°/21 mm. Rathke (*Annalen*, 1869, **152**, 216) gives 77—78°/16 mm. Di-*n*-propyl diselenide (50% yield) had constant b. p. 105°/11 mm. Tschugaeff (*Ber.*, 1909, **42**, 49) gives 99°/13 mm.

Fission of Dimethyl Diselenide.—(a) *By mercuric cyanide.* When the diselenide was added to excess of 5% aqueous mercuric cyanide, a yellow solid separated which contained nitrogen. This could not be crystallised from any solvent owing to its insolubility. It decomposed at 101° with frothing and turned black. No odour of an alkyl selenium compound was observed on warming with hydrochloric acid or sodium hydroxide. The filtrate from this precipitate was extracted with ether, yielding a few drops of oil, b. p. *ca.* 150°, having a characteristic odour. Direct comparison with methyl selenocyanate, b. p. 155° (Stolte, *Ber.*, 1886, **19**, 1577, gives 158°), showed the odours to be identical. When the fission was repeated in aqueous alcoholic solution, 1·2 g. of dimethyl diselenide being used, 1·3 g. of the yellow precipitate, presumably $CH_3 \cdot Se \cdot HgCN$, was obtained. Calc., 2·0 g. On keeping, it darkened, finally giving an odourless black powder containing mercury and selenium.

(b) *Fission by acidified mercuric chloride.* Addition of dimethyl diselenide alone or in alcohol to Biginelli's solution (mercuric chloride, 10 g.; water, 80 c.c.; hydrochloric acid, 20 c.c.) gave yellow insoluble needles, m. p. 123° (Found : Cl, 16·4. $CH_3SeClHg,HgCl_2$ requires Cl, 17·7%). The product probably contained some $CH_3 \cdot Se \cdot HgCl$.

When dimethyl diselenide was aerated first through mercuric cyanide and then through Biginelli's solution, it was completely retained by the cyanide and no trace of precipitate formed in the acid mercuric chloride, indicating the absence of monoselenide from the specimen.

Di-*n*-propyl diselenide, when aerated into mercuric cyanide or Biginelli's solution for several hours, gave no precipitate. Direct addition to alcoholic mercuric cyanide slowly gave a yellow solid, m. p. 138° (decomp.). It was not further examined.

Methyl Ethyl Selenide Mercurichlorides.—Dimethyl diselenide was dissolved in alcohol and treated with just over two atomic proportions of sodium, giving an orange solution and a black precipitate. On addition of ethyl iodide (2 mols.) reaction occurred at once. The clear yellow solution was refluxed for 30 mins., water added, and the mixture distilled in steam. The yellow distillate contained a little unchanged diselenide and, judging from the odour, a monoselenide also. Volatile matter was removed in an air stream through mercuric cyanide (to remove dimethyl diselenide) into Biginelli's solution, where white needles formed, m. p. 98°, decomposing at 140°. After drying in a vacuum, these melted at 100° and decomposed as before. On crystallisation from 3% aqueous mercuric chloride the m. p. was 140° (decomp.) (probably a higher mercurichloride) and from 50% alcohol 100°. This product was dried over sulphuric acid (Found : Hg, 51·8; Cl, 18·0. $C_3H_8Cl_2HgSe$ requires Hg, 52·3; Cl, 18·0%).

The preparation was repeated, diethyl diselenide, alcohol, sodium, and methyl iodide being used. Aspiration through Biginelli's solution as before gave the same product, m. p. and mixed m. p. 100°. $(CH_3)_2Se,HgCl_2$ melts at 153° (decomp.), and $(C_2H_5)_2Se,HgCl_2$ at 93°. An equimolecular mixture had m. p. 80—87°.

Although the methyl ethyl selenide mercurichloride, m. p. 140°, had been obtained by two different methods, the

experiments were on a very small scale. It therefore appeared desirable to confirm these results, especially in view of the formation of a black precipitate which may have been selenium, capable of giving rise to some sodium selenide and hence to dimethyl selenide. The following experiment, however, fully confirmed the earlier ones.

Dimethyl diselenide (19·4 g.; 1 mol.) in dry ether (40 c.c.) was added to sodium shavings (15 g.; 6 atoms) covered with dry ether (160 c.c.), in a flask cooled in water and carrying a reflux condenser connected to wash-bottles containing mercuric chloride to prevent escape of vapours. Alcohol (70 c.c.) was slowly added, giving a steady effervescence and a red turbidity. A slow stream of nitrogen was passed through to avoid oxidation of the sodium methylselenothiol. Ethyl bromide (80 g.; 6 mols.) was slowly added and also a further 20 c.c. of alcohol to ensure removal of all the sodium. Sodium bromide separated and the red colour disappeared entirely. Next day the mixture was refluxed for an hour, and most of the ether then removed with a column (Ether-Selenide Fraction I). On continuing distillation on the steam-bath without a column Fraction II was obtained. Addition of water to the pasty residue gave an oil. This was extracted with ether, and the dried extract repeatedly fractionated, finally yielding Fraction III.

Test portions of the three fractions were separately treated with aqueous mercuric chloride, and the resulting mercurichlorides carefully examined by repeated recrystallisation from (*a*) alcohol and (*b*) aqueous mercuric chloride. Determinations of m. p. and mixed m. p. showed them to be essentially the same. From (*a*) the m. p. was 100° and from (*b*) 141·5° (decomp.) in close agreement with the results obtained in the small-scale experiments.

As a further check the three ether-selenide fractions were mixed and added to excess of aqueous mercuric chloride. The resulting solid W (as in all these experiments) was initially a mixture of the two mercurichlorides of methyl ethyl selenide. Repeated recrystallisation of a portion from aqueous mercuric chloride gave a homogeneous product, m. p. 141·5° (decomp.).

Finally the bulk of the mixture W (50 g.) was decomposed with excess of aqueous sodium hydroxide, and the liberated methyl ethyl selenide distilled from a steam-bath and dried over calcium chloride. Repeated distillation showed the product to be homogeneous, b. p. 86—87°. The slight amounts remaining in the flask each time were united and redistilled, b. p. 86—90°. Methyl ethyl selenide boils at 86° (Tschugaeff, *loc. cit.*). A few drops when added to excess of mercuric chloride gave a product, m. p. 141·5° (decomp.) (Found: Cl, 21·7. $CH_3{\cdot}Se{\cdot}C_2H_5{,}2HgCl_2$ requires Cl, 21·4%). This convenient method obviates the use of hydrogen selenide and the isolation of the selenothiol. *Methyl ethyl selenide dimercurichloride* is stable in air, but the monomercurichloride gradually loses dimethyl selenide with formation of some dimercurichloride and consequent rise in m. p. When decomposed with sodium hydroxide, the resulting yellow mercuric oxide is not reduced by the selenide even at 100°. Alkyl selenides differ in this respect from trialkylarsines (Challenger, Higginbottom, and Ellis, J., 1933, 99) and from dimethyl telluride (Bird and Challenger, J., 1939, 166).

Methyl n-*Propyl Selenide Mercurichloride.*—The preparation was analogous to that of the methyl ethyl compound. Both dimethyl diselenide and di-*n*-propyl diselenide were used as starting points and the mercurichloride had the same m. p. (87°) in each case. On recrystallisation from alcohol the m. p. was 88° (Found: Hg, 49·2; Cl, 17·8. $C_4H_{10}Cl_2HgSe$ requires Hg, 49·2; Cl, 17·5%). With neutral mercuric chloride as absorbent the product melted at 160° (decomp.) but was not analysed. *Di-*n*-propyl selenide mercurichloride*, whether formed from its ingredients in aqueous alcoholic solution or in Biginelli's solution, melts at 93—94° after recrystallisation from alcohol (Found: Hg, 45·1. $C_6H_{14}Cl_2HgSe$ requires Hg, 45·8%). In admixture with methyl *n*-propyl selenide mercurichloride the m. p. was 70—85°.

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114. *Studies in Biological Methylation. Part IX.* The Action of* Scopulariopsis brevicaulis *and certain* Penicillia *on Salts of Aliphatic Seleninic and Selenonic Acids.*

By MARJORIE L. BIRD and FREDERICK CHALLENGER.

Addition of the sodium salts of methane-, ethane-, and propane-1-seleninic acids or their hydrogen nitrates to bread cultures of *Scopulariopsis brevicaulis* and of certain *Penicillia* gives dimethyl, methyl ethyl, and methyl *n*-propyl selenides respectively. Addition of the potassium salts of the corresponding selenonic acids $R{\cdot}SeO_2{\cdot}OK$ to similar cultures gives only dimethyl selenide, owing to hydrolysis of the selenonates to ROH and $KHSeO_3$. The bearing of these results on the hypothesis put forward by Challenger (see below) to explain the phenomenon of methylation, and particularly the conversion of selenites and selenates into dimethyl selenide, by certain moulds, is discussed.

IN Part VIII a hypothesis was proposed (Challenger, *Chem. and Ind.*, 1942, in the press) to account for most of the observed cases of biological methylation in animals and in moulds. On this view methaneselenonic acid, $CH_3{\cdot}SeO_2{\cdot}OH$, methaneseleninic acid, $CH_3{\cdot}SeO_2H$, dimethylselenone, $(CH_3)_2SeO_2$, and dimethyl selenoxide, $(CH_3)_2SeO$, may be intermediate stages in the conversion of selenious acid or its salts into dimethyl selenide by *Scopulariopsis brevicaulis*. The process might be initiated by the transfer of a methyl group from some compound such as choline, betaine, or methionine.

The present communication describes experiments designed to test the behaviour of the first two of the postulated intermediates in bread cultures of *S. brevicaulis* and of certain other moulds, all of which have been found by us (J., 1939, 163) to convert tellurites and tellurates into dimethyl telluride. The nitrate of dimethyl selenoxide has already been shown by one of us and North (J., 1934, 68) to give dimethyl selenide with *S. brevicaulis*.

Volatile products from the cultures were aspirated through aqueous mercuric cyanide to remove alkylselenothiols and diselenides and then through Biginelli's solution (mercuric chloride, 10 g.; water, 80 c.c., hydrochloric acid, 20 c.c.) to remove dialkyl selenides.

* Parts I (J., 1933, 95) to VII (J., 1939, 163) of this series were published under the title "The Formation of Organometalloidal and Similar Compounds by Micro-organisms." The revised title more clearly indicates the scope of the investigation.

The behaviour of potassium methaneselenonate (preceding paper) would at first appear to be in agreement with the hypothesis outlined above, since with *S. brevicaulis*, *Penicillium chrysogenum*, *P. notatum*, and the green Penicillium allied to *P. notatum* (J., 1939, 163) dimethyl selenide was produced in small amount. This might have arisen in at least three ways: (*a*) according to the suggested mechanism; (*b*) by a rearrangement of potassium methaneselenonate, thus: $2CH_3{\cdot}SeO_2{\cdot}OK = (CH_3)_2SeO_2 + K_2SeO_4$, when the selenate would be methylated and the (unknown) selenone might be reduced, giving dimethyl selenide in each case. Finally (*c*) hydrolysis with elimination of methyl alcohol would yield potassium hydrogen selenite, which would then give dimethyl selenide (Challenger and North, *loc. cit.*). Addition of potassium ethaneselenonate and propane-1-selenonate to cultures of these moulds showed that (*c*) is the correct explanation, dimethyl selenide being obtained in each case. With these substrates methyl ethyl and methyl *n*-propyl selenides should have been obtained according to (*a*), whereas process (*b*) should have yielded a mixture of dimethyl selenide with diethyl selenide and di-*n*-propyl selenide respectively. The results with the three potassium alkaneselenonates are due to the instability of these compounds to hydrolysing agents (preceding paper) but are strikingly differentiated from the behaviour of the mono- and di-alkylarsonic acids $R{\cdot}AsO(OH)_2$ and $R_2AsO{\cdot}OH$. These compounds are very stable and invariably undergo methylation, giving $RAsMe_2$ and R_2AsMe, respectively, no trace of trimethylarsine being evolved except where $R = CH_3$ (see Challenger *et al.*, J., 1933, 95; 1935, 396; 1936, 264). It is not, however, impossible that methaneselenonic acid may be an intermediate in the conversion of inorganic selenite or selenate into dimethyl selenide, since it might be sufficiently stable to pass on to the next stage without loss of selenite when actually formed in the mould cell.

The salts of the alkaneseleninic acids $R{\cdot}SeO_2H$ (R = Me, Et or *n*-Pr) with most of the moulds mentioned above give the corresponding alkyl methyl selenides $R{\cdot}Se{\cdot}CH_3$. In the case of the methane- and ethane-seleninates the selenide was accompanied by either methyl- and ethyl-selenothiol R·SeH or the corresponding diselenide. Fredga (Dissert., Uppsala, 1935) states that seleninic acids give selenium and diselenides on decomposition, but no details are available. Cyanomercury methylselenothiol Me·Se·HgCN and (probably) mercury diethylselenothiol $(EtSe)_2Hg$ respectively separated in the mercuric cyanide absorption tubes, and alkyl selenocyanate was produced: $R{\cdot}Se{\cdot}SeR + Hg(CN)_2 = R{\cdot}Se{\cdot}HgCN + R{\cdot}SeCN$ (see preceding paper). Owing to the ready oxidation of RSeH (Tschugaeff, *Ber.*, 1909, **42**, 49) the reaction in the mercuric cyanide is probably due to diselenide.

The formation of dimethyl and methyl alkyl selenides from salts of the seleninic acids is in agreement with the suggested scheme in which methaneseleninic acid is an intermediate product. Dimethyl selenide might conceivably arise from methaneseleninic acid thus: $2CH_3{\cdot}SeO_2H = (CH_3)_2Se + H_2SeO_4$; this was not observed in control experiments using uninoculated bread, nor does it seem to be recorded in the literature. Such a decomposition of ethane- and propane-1-seleninic acids in the mould cultures would give a mixture of dimethyl selenide with diethyl and di-*n*-propyl selenides respectively. This was never observed, the mercuric chloride of the methyl alkyl selenide separating in a pure condition in the absorption tubes.

The production of diethyl diselenide or ethylselenothiol in cultures containing potassium ethaneseleninate creates some slight ambiguity. By analogy with the behaviour of alkylthiols and disulphides (Challenger and Rawlings, J., 1937, 868; Challenger and Blackburn, J., 1938, 1872) either of these compounds might yield methyl ethyl selenide without passing through the selenone $(CH_3{\cdot}SeO_2{\cdot}C_2H_5)$ stage. The behaviour of alkylselenothiols in bread cultures was not studied, but the diselenides gave no methyl alkyl selenides in such cultures.

In the conversion of sodium selenite into dimethyl selenide by *S. brevicaulis* red selenium is produced and with numerous moulds and bacteria selenium is deposited within the organisms (Gosio, *Atti R. Accad. Lincei*, 1904, **13**, I, 642). Sodium selenate readily gives dimethyl selenide with *S. brevicaulis* but no selenium is produced.

According to the hypothesis cited on p. 574, selenate is first reduced to selenite before attachment of the methyl group. If so, it is surprising that the resulting selenite escapes reduction to selenium, unless attachment of methyl occurs so rapidly in the cell as to obviate this.

An alternative mechanism might appear possible. Dimethyl selenate $(MeO)_2SeO_2$ might be produced from the selenate ion and its reduction to dimethyl selenite $(MeO)_2SeO$, followed by isomerisation to the methyl ester of methaneselenonic acid $Me{\cdot}SeO_2{\cdot}OMe$. The methaneselenonic acid resulting on hydrolysis could then react according to the original scheme. Dimethyl selenite (Michaelis and Landmann, *Annalen*, 1887, **241**, 159) is, however, readily decomposed by water, giving selenious acid, and Strecker and Daniel (*ibid.*, 1928, **462**, 189) failed to observe any isomerisation of dialkyl selenites to alkyl esters of the alkaneselenonic acids. Nevertheless the formation of derivatives of methyl methanesulphonate on heating dimethyl sulphite with glycine (Voss and Wulkan, *Ber.*, 1937, **70**, 390) and with dimethylaniline or pyridine (Voss and Blanke, *Annalen*, 1931, **485**, 258) suggests that isomerisation of dimethyl selenite may not be impossible.

Experimental.

The strain of *Scopulariopsis brevicaulis* (*Penicillium brevicaule*) used is registered in the Baarn List of Fungi 1932 as *S. brevicaulis* (Sacc.) Bainier. In one experiment only the strain *S. brevicaulis* Saccardo (strain Washington 2) was used. Details of these strains, designated for convenience (A) and (D), are recorded by Challenger, Higginbottom, and Ellis (*loc. cit.*, p. 98). The strains of *Penicillium chrysogenum*, *P. notatum* and the green Penicillium (closely allied to *P. notatum*) were those used by us in an earlier investigation (J., 1939, 163). Bread crumbs, slightly moistened with water, were placed in test-tubes of about 40 c.c. capacity so as to fill ⅔ of the space, or in 250 c.c. conical flasks, 40 g.

in each. Sterilisation of the media, apparatus, and stopper with delivery tubes and of the air stream was ensured as before (J., 1933, 98). The seleninic acids were used as their sodium salts or as the sodium salts of their hydrogen nitrates, the selenonic acids as the potassium salts. Owing to their instability these compounds were not sterilised, but solutions in sterile water (0·15—0·2 g. in 2 c.c.) were used. The mould was allowed to form a good mycelium before the substrates were added; the time required was usually 2 days at 32° and 2 at room temperature for *S. brevicaulis*, 3 days at room temperature for *P. chrysogenum* and the "variety" of *P. notatum*, and 5—6 days at room temperature for *P. notatum*. Volatile products produced in the cultures were aspirated by sterile air through aqueous mercuric cyanide (5%, 5 c.c.) and then through Biginelli's solution (5 c.c.) contained in small tubes. Control experiments showed that addition of the sodium or potassium salts of all the seleninic or selenonic acids used in this work to tubes of sterile bread crumbs, followed by aeration for as long as 2 months into mercuric cyanide and Biginelli's solution in series, gave no precipitate. No odour was detected in these control flasks and no selenium was deposited in the media.

S. brevicaulis (*Strain D*) *and the Sodium Salt of Methaneseleninic Acid Hydrogen Nitrate.*—(Five tubes). After 3 days traces of a yellow precipitate, probably CH_3·Hg·SeCN (m. p. 101° decomp.), formed in the mercuric cyanide and a white precipitate in the Biginelli's solution (0·05 g. after 10 days, when the experiment was discontinued). This had m. p. and mixed m. p. 153° with authentic dimethyl selenide mercurichloride of m. p. 153°—all with decomposition. The mercuric cyanide solution had an odour of methyl selenocyanate. Some orange crystals (0·04 g.) appeared in the Biginelli's solution later in the experiment. These had m. p. and mixed m. p. 123° (decomp.) with the product of the same m. p. obtained on aeration of dimethyl diselenide into Biginelli's solution (preceding paper).

S. brevicaulis (Strain A) in a similar experiment using sodium methaneseleninate (six tubes) gave after 6 weeks 0·07 g. of dimethyl selenide mercurichloride, m. p. and mixed m. p. 153° (decomp.), and 0·1 g. of the yellow crystals, m. p. and mixed m. p. 101°, with the product of the same m. p. obtained from dimethyl diselenide and mercuric cyanide (Bird and Challenger, *loc. cit.*).

S. brevicaulis *and the Sodium Salt of Ethaneseleninic Acid Hydrogen Nitrate.*—(Five tubes). In 2 days small amounts of yellow solid, sintering from 85° and blackening and decomposing at 130°, formed in the mercuric cyanide, which then smelled strongly of an alkyl selenocyanate. In the Biginelli's solution a white solid, m. p. and mixed m. p. 100°, with methyl ethyl selenide mercurichloride, m. p. 100°, was deposited. Three weeks' aeration produced very little more solid.

S. brevicaulis *and the Sodium Salt of Propane-1-seleninic Acid Hydrogen Nitrate.*—(Seven tubes). No trace of yellow solid formed in the mercuric cyanide during 6 weeks, but, after 5, 25, and 35 days respectively, deposits of 0·025 g., 0·04 g., and 0·01 g. of white crystals formed in the Biginelli's solution. These all melted at 88° and the first deposit did not depress the m. p. (88°) of an authentic specimen of methyl *n*-propyl selenide mercurichloride. Replacement of the Biginelli's solution by neutral aqueous mercuric chloride (4%) gave a white deposit of m. p. and mixed m. p. 160° (decomp.) with the compound of the same m. p. obtained similarly from methyl *n*-propyl selenide (Bird and Challenger, *loc. cit.*).

Penicillium notatum *and the Seleninic Acids.*—The sodium salts of methaneseleninic hydrogen nitrate and of ethaneseleninic acid being used, no methylation was observed during 3—4 weeks, no trace of deposit being formed in the Biginelli's solution. The characteristic yellow precipitates were obtained in the mercuric cyanide after 14—48 hrs. from the commencement of the experiment, that from the methyl compound (0·02 g.) decomposing at 101° with previous softening at 90°, and that from the ethyl derivative (0·12 g.) having m. p. 85°. This experiment was repeated and the yellow solid had m. p. and mixed m. p. 85° (decomp. 130°) with that obtained directly from authentic diethyl diselenide and mercuric cyanide. Alkyl selenocyanate odour in the mercuric cyanide was very strong in both experiments with the ethyl compounds (see above).

Four flask cultures containing the sodium salt of propane-1-seleninic acid hydrogen nitrate gave no deposit or odour in the mercuric cyanide during 5 weeks. The deposit in Biginelli's solution (0·06 g. in 8 days) had m. p. and mixed m. p. 86—87° with methyl *n*-propyl selenide mercurichloride. A further deposit (0·07 g.) was removed on the 21st day and had m. p. and mixed m. p. 85·5°.

The green Penicillium allied to P. notatum *and the Three Seleninic Acids.*—Three tube cultures of sodium methaneseleninate gave no dimethyl selenide after 19 days, but the usual deposit, m. p. 101°, and an odour of methyl selenocyanate formed in the mercuric cyanide. Undoubted methylation was observed with the sodium salts of the hydrogen nitrates of the ethyl and *n*-propyl derivatives, 3 flask cultures being used in each case. 0·13 G. of methyl ethyl selenide mercurichloride (white needles), m. p. and mixed m. p. 100°, formed in Biginelli's solution in 4 days, and in the same time 0·03 g. and in 3 weeks 0·2 g. of methyl *n*-propyl selenide mercurichloride, m. p. and mixed m. p. 88°, were similarly obtained.

A second experiment was carried out with this mould and the sodium salt of ethaneseleninic acid hydrogen nitrate. The resulting mercurichloride, m. p. and mixed m. p. 100° as before, was recrystallised from 3·5% aqueous mercuric chloride; it then melted at 141·5° (decomp.), a figure which was unchanged by three further crystallisations, indicating its homogeneity. This melted at 140—141° (decomp.) in admixture with an authentic specimen of methyl ethyl selenide dimercurichloride, m. p. 140—141° (decomp.).

P. chrysogenum *and the Seleninic Acids.*—No methylation was observed with the sodium salt of methaneseleninic acid (6 tubes; 4 weeks), but the usual yellow solid, m. p. 101° (decomp.), and odour of methyl selenocyanate formed in the mercuric cyanide. With the sodium salt of ethaneseleninic acid hydrogen nitrate and the corresponding *n*-propyl derivative (3 tubes) methylation occurred and methyl ethyl selenide mercurichloride (0·075 g., m. p. and mixed m. p. 100°) and methyl *n*-propyl selenide mercurichloride (0·15 g., m. p. and mixed m. p. 88°) separated from the Biginelli's solution. As usual, no odour or deposit was produced in the cyanide from the *n*-propyl compound, but 0·015 g. of yellow solid, m. p. 85°, and an odour of alkyl selenocyanate were formed from the ethaneseleninic acid salt.

S. brevicaulis *and Potassium Methaneselenonate.*—(Four flasks). After 9 days a slight deposit, m. p. 153—155° (decomp.), formed in the Biginelli's solution. After 9 weeks a further small amount, sintering at 145° and melting at 155° (decomp.), was removed. This, on recrystallisation from acetone, had m. p. and mixed m. p. 153° (decomp.) with dimethyl selenide mercurichloride. During this period only a trace of yellow deposit, blackening after a week or two, formed in the mercuric cyanide. The experiment was repeated, but after 7 weeks the deposits which formed were too small to remove.

S. brevicaulis *and Potassium Ethaneselenonate.*—(Four flasks). During 8 weeks only traces of a yellow deposit, quickly blackening, formed in the cyanide tubes and some white crystals in Biginelli's solution. Their quantity was just sufficient for a m. p. and mixed m. p. (151—153° decomp.) with dimethyl selenide mercurichloride.

S. brevicaulis *and Potassium Propane-1-selenonate.*—(Six tubes). No deposit formed in the cyanide during 3 weeks, but 0·001 g. of white crystals, m. p. and mixed m. p. 150—153° (decomp.) with dimethyl selenide mercurichloride, formed in the Biginelli's solution.

P. chrysogenum *and the Potassium Salts of the Three Selenonic Acids.*—(Five tubes in each case. Duration, 7 weeks). No odour of alkyl selenocyanate or precipitate was produced in the mercuric cyanide during 7 weeks, although in the case of the methyl compound the solution became clear brownish-yellow. Dimethyl selenide mercurichloride separated

from the Biginelli's solution in each case, the amount from the methaneselenonate being only sufficient for the determination of m. p. and mixed m. p. 153°. The other two salts gave 0·08 g. and 0·075 g. respectively.

The Green Penicillium allied to P. notatum.—This gave similar results with the three selenonates. Four tube cultures were used for the methyl and ethyl compounds and 3 flask cultures for the *n*-propyl derivative. There was no deposit in the cyanide and after 3 weeks the weights and m. p.'s of the dimethyl selenide mercurichloride were (*a*) 0·007 g., 150—152° (decomp.); (*b*) 0·001 g., 152—153° (decomp.); and (*c*) 0·005 g., 150° (decomp.) and mixed m. p. 153° (decomp.).

P. notatum *and the Potassium Salts of the Three Selenonic Acids.*—(Methyl and ethyl compounds, 3 flask cultures; *n*-propyl compound, 4 tube cultures). In each case only a trace of precipitate was obtained in the Biginelli's solution. A m. p. determination (155° decomp.) was possible with that from the ethyl compound. In the other cases the precipitate gave an odour of dimethyl selenide on treatment with sodium hydroxide. Traces only of yellow precipitate formed in the mercuric cyanide from the methyl and the ethyl derivative and none with the *n*-propyl compound during 2—4 weeks. Odour of selenocyanate was absent.

S. brevicaulis (*Strain A*) *and Sodium Benzeneseleninate.*—Six tube cultures on bread were used and the benzeneseleninate, dissolved in sterile water, was added. In a few days a strong odour closely resembling that of phenyl methyl selenide, prepared for comparison, was observed. Aspiration for 6 weeks into concentrated nitric acid yielded, however, only ammonium nitrate containing, by the flame test, traces of a selenium compound. Repetition, cultures on aqueous 3% glucose–Czapek-Dox medium being used, also gave a strong odour in 3 days. After 4—6 weeks, extraction of the medium and of the mycelium with chloroform yielded respectively a slight residue and diphenyl diselenide, m. p. 60° and mixed m. p. 61° with an authentic specimen of m. p. 61°.

In control experiments on the liquid medium no odour was produced during 2 months.

The decomposition of the seleninic acid into the diselenide in cultures of the mould may prevent the formation of more than traces of phenyl methyl selenide, which, moreover, is difficulty volatile.

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115. *Synthesis and Anti-bacterial Properties of Alkyl and Alkenyl Derivatives of 2 : 6-Dimethoxybenzoquinone.*

By ALBERT EDWARD OXFORD.

A number of 3-alkyl, 3-alkenyl, and 3 : 5-dialkyl derivatives of 2 : 6-dimethoxybenzoquinone (I) have been prepared by the action of appropriate diacyl peroxides on (I), and the anti-bacterial powers of these quinones against *Staphylococcus aureus* have been compared.

FIESER and OXFORD (*J. Amer. Chem. Soc.*, 1942, **64**, in the press) prepared a number of alkyl- and alkenyl-substituted benzo- and naphtha-quinones by the reaction RH(quinone) + Alk·CO·O·O·CO·Alk = R·Alk + Alk·CO_2H + CO_2, the yields varying from a trace up to 60%. It has recently been discovered that 2 : 6-dimethoxybenzoquinone and 4 : 6-dimethoxytoluquinone are powerful inhibitors of the growth of *Staphylococcus aureus in vitro* (Oxford, *Chem. and Ind.*, 1942, **61**, 189), and it became of interest to prepare other alkyl derivatives of 2 : 6-dimethoxybenzoquinone with two side chains, and also with side chains longer than methyl, in order that their anti-bacterial action might be compared with that of the simpler quinones. This has now been accomplished by an application of the above reaction on the readily accessible 2 : 6-dimethoxybenzoquinone (see Baker, J., 1941, 665). An excess of this quinone was used if only one side chain was to be introduced, but for the introduction of two side chains a little more than the theoretical amount of the peroxide was found to be suitable. The following have thus been prepared with ease: 3-ethyl-, 3-*n*-propyl-, 3-propenyl-, 3-*iso*butyl-, and 3 : 5-dimethyl-2 : 6-dimethoxybenzoquinone. An attempt to prepare the 3 : 5-diethyl derivative yielded an uncrystallisable oil, undoubtedly containing this substance, which could not easily be further purified. The reaction failed with di*iso*butyryl and disuccinyl peroxides.

Although the yields in this application of the above reaction are small (15% or less), the separation of the alkylquinone from the water-soluble fatty acid and from unchanged 2 : 6-dimethoxybenzoquinone is readily accomplished by extraction of the aqueous acetic acid reaction mixture with cold light petroleum, in which the last-named quinone, unlike its homologues, is insoluble. None of the new quinones is markedly more active against *Staph. aureus* than 4 : 6-dimethoxytoluquinone; indeed the 3-propenyl derivative is considerably less active.

EXPERIMENTAL.

Diacetyl, dipropionyl, and di-*n*-butyryl peroxides were prepared from the corresponding acid anhydrides by the method of Gambarjan (*Ber.*, 1909, **42**, 4010), light petroleum (b. p. 40—60°) being used as the diluent in the last instance in place of ether. Di*iso*butyryl, dicrotonyl, and di*iso*valeryl peroxides were prepared from the corresponding acid chlorides essentially by the method of Price, Kell, and Krebs (*J. Amer. Chem. Soc.*, 1942, **64**, 1103) save that light petroleum (b. p. 40—60°) was used as diluent in place of benzene. In all instances the diluent was allowed to evaporate spontaneously at room-temperature immediately before use of the peroxide. Dicrotonyl peroxide, thus prepared, melts at about 34°; Clover and Richmond (*Amer. Chem. J.*, 1903, **29**, 194) record m. p. 41°.

The following description of the preparation of 2 : 6-dimethoxy-3-ethylbenzoquinone is typical of the method used for the introduction of one side chain. To a solution of dipropionyl peroxide (1·0 g.) in glacial acetic acid (60 ml.) was added 2 : 6-dimethoxybenzoquinone (1·25 g.; 9% excess), and the whole slowly heated with stirring (in a water-bath) until the temperature had reached 80° and the quinone had dissolved. The temperature of the bath was then raised to 100° and maintained until the addition of a piece of porous pot to the glacial acetic acid solution showed that effervescence had ceased (15—30 minutes). The cooled solution was diluted with water (300 ml.) and extracted twice with light petroleum (once only for the higher homologues and four times for the propenyl derivative). The unchanged 2 : 6-dimethoxybenzoquinone may then be recovered by filtration of the aqueous layer. The extract was dried over anhydrous

sodium sulphate and concentrated to small volume, and the remainder of the solvent allowed to evaporate spontaneously. The slightly gummy, crystalline residue was pressed on a porous plate and recrystallised from a little light petroleum (b. p. 80—100°); yield, 0·12 g. The higher homologues, being readily soluble in cold light petroleum, were crystallised from aqueous methanol. The propenyl derivative was repeatedly crystallised from light petroleum at 0°.

For the preparation of 2 : 6-dimethoxy-3 : 5-dimethylbenzoquinone the quantities were: 2 : 6-dimethoxybenzoquinone (2·0 g.), diacetyl peroxide (3·0 g.; 7% excess), and glacial acetic acid (100 ml.). A corresponding experiment with dipropionyl peroxide yielded a completely oily product which resisted all attempts at crystallisation. It had considerable anti-bacterial activity (see table) and, like 2 : 6-dimethoxy-3 : 5-dimethylbenzoquinone, gave a deep blue colour with concentrated sulphuric acid. The monosubstituted alkyl-quinones gave a blue colour with a marked violet tinge with this reagent, but the propenyl derivative gave merely a brown colour. The last-named, which was much more intensely coloured than the other quinones, gave also a much bluer colour with dilute caustic soda solution on warming.

The physical and anti-bacterial properties of this series of quinones are summarised in the table. For the tests against *Staph. aureus*, sterile aqueous solutions containing usually 30—100 parts per million were made up and added to sterile heart broth and 2% glucose broth as described by Oxford (*Chem. and Ind.*, 1942, **61**, 48). The test organisms were three strains of *Staph. aureus* numbered 3095, 3750, and 3761 in the National Collection of Type Cultures (Lister Institute), and the inoculum given to each tube was always 500—1000 viable bacteria per ml. Dilute aqueous solutions of these quinones, which are only very sparingly soluble in water, seem perfectly stable for long periods at room temperature in diffuse daylight.

TABLE.

Derivative of 2 : 6-dimethoxy-benzoquinone.	Crystalline appearance and m. p.	Analytical data: Found, % (micro-analyses by Drs. Weiler and Strauss, Oxford).	Analytical data: Calc., %.	μg. per ml. completely inhibiting *Staphylococcus aureus*: N.C.T.C. No. 3095 in glucose broth for 1 day (A) and 2 days (B) at 37°.	N.C.T.C. No. 3750 in glucose broth for 1 day (A) and 2 days (B) at 37°.	N.C.T.C. No. 3761 in standard heart broth for 1 day (A) and 2 days (B) at 37°.
Unsubstituted	Yellow needles, 255°	Graebe and Hess, *Annalen*, 1905, **340**, 237.		2·5 (A) 12·5 (B)	3·7 (A) 21·0 (B)	12·5 (A) 21·0 (B)
3-Methyl- (*i.e.*, 4 : 6-dimethoxytoluquinone)	Yellow needles, 125°	Anslow, Ashley, and Raistrick, J., 1938, 439; see also Fieser and Oxford, *loc. cit.*		1·7 (A) 3·3 (B)	1·7 (A) 3·3 (B)	3·3 (A) 10·0 (B)
3-*Ethyl*-, $C_{10}H_{12}O_4$	Small yellow plates, 59°	C, 61·1 H, 6·2	C, 61·2 H, 6·2	1·8 (A) 3·6 (B)	1·8 (A) 1·8 (B)	1·8 (A) 9·1 (B)
3-n-*Propyl*-, $C_{11}H_{14}O_4$	Yellow plates and needles, 20°	C, 63·6 H, 7·1	C, 62·8 H, 6·7	2·9 (A) 5·9 (B)	2·9 (A) 2·9 (B)	5·9 (A) 9·8 (B)
3-iso*Butyl*-, $C_{12}H_{16}O_4$	Yellow needles, 50—51°	C, 64·4 H, 7·1	C, 64·3 H, 7·2	2·0 (A) 4·0 (B)	4·0 (A) 4·0 (B)	4·0 (A) 4·0 (B)
3-*Propenyl*-, $C_{11}H_{12}O_4$	Orange-red needles, 84°	C, 63·4 H, 5·7 OMe, 30·1	C, 63·4 H, 5·8 OMe, 29·8	7·1 (A) 24·0 (B)	7·1 (A) 24·0 (B)	7·1 (A) 24·0 (B)
3 : 5-*Dimethyl*-, $C_{10}H_{12}O_4$	Orange-yellow plates, 134°	C, 61·4 H, 6·4	C, 61·2 H, 6·2	3·2 (A) 3·2 (B)	1·6 (A) 3·2 (B)	3·2 (A) 3·2 (B)
3 : 5-*Diethyl*-	Yellow oil	Not obtained pure		9·1 (A)	9·1 (A) 9·1 (B)	9·1 (A)

The unexpected failure of the reaction with di*iso*butyryl peroxide was at first thought to be due to the greater stability of this peroxide, which, when heated in a narrow tube, decomposes vigorously at 110—120°, *i.e.*, 20° higher than the corresponding decomposition point for di-*n*-butyryl peroxide. No trace of quinone soluble in light petroleum was obtained, however, when the reaction with 2 : 6-dimethoxybenzoquinone was carried out at the b. p. of glacial acetic acid instead of 100°. This peroxide differs from the rest in having substituents attached to the α-carbon atoms. No trace of quinone soluble in sodium bicarbonate solution was formed when disuccinyl peroxide (Clover and Houghton, *Amer. Chem. J.*, 1904, **32**, 55) was caused to react in glacial acetic acid solution at 100° with 2 : 6-dimethoxybenzoquinone.

The work is being continued, particularly in the direction of the introduction of other unsaturated side chains, and also of the finding of the optimum conditions for the alkylation of quinones by this method.

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116. *A New Method of End-group Assay for Laminarin and similarly constituted Polysaccharides.*

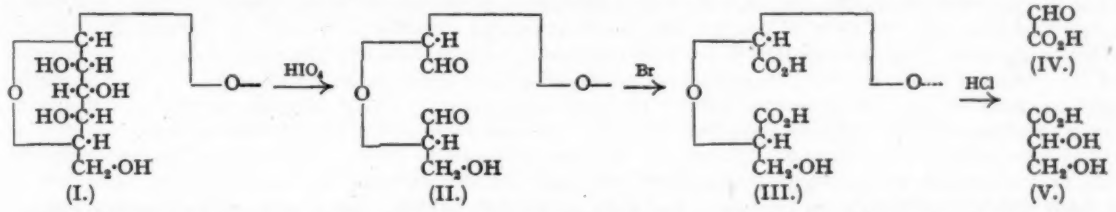
By VINCENT C. BARRY.

Periodic acid attacks only the non-aldehydic end-groups of laminarin, introducing into each of these two aldehydo-groups with loss of one carbon atom. Subsequent oxidation with bromine yields a polysaccharide whose end-group now contains two carboxyl groups. Estimation of the dicarboxylated end-group indicates a chain-length of 16 glucose units for laminarin.

IN previous work (Barry, *Sci. Proc. Roy. Dublin Soc.*, 1939, **22**, 59; 1941, **24**, 423), laminarin has been shown to consist for the most part of β-glucopyranose units linked from the aldehydic carbon atom of one glucose unit to carbon atom 3 of the adjacent unit. Regulated hydrolysis of the polysaccharide has been shown to yield,

among other products, a disaccharide, laminaribiose, 3-[β-*d*-glucosido]-*d*-glucose (*loc. cit.*). This 1 : 3 linkage of laminarin, as opposed to the 1 : 4 linkage of cellulose, has been confirmed by the behaviour of laminarin towards periodic acid. The consumption of periodic acid in the latter case is negligible in comparison with what takes place with starch or cellulose (Barry, Dillon, and McGettrick, this vol., p. 183). Nevertheless, a small but definite reduction of the periodic acid takes place and this has now been shown to be due to the oxidation of terminal non-aldehydic glucose units. As these are the only units in the polysaccharide molecule which present a :C(OH)·C(OH): group for attack, it was to be expected that each of these units would be modified as is α-methylglucoside by the periodic acid (Hudson and Jackson, *J. Amer. Chem. Soc.*, 1937, **59**, 2049).

On the assumption that the oxidation takes the same course in both cases, a terminal non-aldehydic glucose unit (I) undergoes cleavage of the carbon chain, as shown, with loss of carbon atom 2. The modified unit (II) now contains two aldehydo-groups, which on further oxidation with bromine are converted into carboxyl groups as shown in (III). The modified end-group can now be assayed directly by neutralisation or alternatively by conversion into the silver salt and estimation of the silver. The results from the two methods are in close agreement and the figures indicate that one terminal non-aldehydic unit is present for every 15 other units.



The oxidised laminarin with its modified end-unit (III) is designated as laminarinic acid. This product on hydrolysis should yield, in addition to glucose, a small quantity of glyoxylic acid (IV) and glyceric acid (V). The presence of glyoxylic acid was shown by the Adamkiewicz–Hopkins–Cole reaction in the hydrolysate obtained by the action of hot dilute hydrochloric acid on laminarinic acid. Also, a small quantity of oxalic acid was produced when laminarinic acid was hydrolysed and the neutralised hydrolysate oxidised subsequently with bromine.

Further confirmation was afforded by hydrolysing the dialdehydic laminarin (II) and treating the neutral hydrolysate with phenylhydrazine acetate. In the cold a small amount of glyoxalphenylosazone was obtained. No such result was obtained when unoxidised laminarin was treated in a similar way. The recognition of glyoxal in this case and of glyoxylic and oxalic acids above, confirms the mechanism of the oxidation as outlined. The dialdehydic laminarin showed no greater reactivity towards alkaline hypoiodite than did laminarin itself.

Oxidation of the laminarin need not proceed for more than 4 or 5 days with 0·25M-periodic acid in order to effect complete modification of the end-units to the dialdehydic form. In one experiment the oxidation was continued for 10 weeks without causing any alteration in acid value of the subsequently produced laminarinic acid. Longer standing with the reagent caused a partial oxidation of the aldehydo-groups to carboxyl. Similar behaviour was indicated by parallel experiments with starch and cellulose. Both of these polysaccharides on standing for 5 days with 0·25M-periodic acid gave products with neutralisation equivalents of about 145, indicating that about two-thirds of the aldehydo-groups introduced by the reagent were already further oxidised to carboxyl. When the untreated laminarin was subjected to the action of bromine of the same strength and under the same conditions as are applied in the conversion of the dialdehyde into laminarinic acid, the recovered laminarin had a definite neutralisation value and apparently a fixed amount of carboxyl had been introduced into the molecule. A second treatment with bromine did not increase the carboxyl content of the polysaccharide. It is probable that oxidation takes place of some of the terminal aldehyde units to modified carboxylated units. Allowance was made for this carboxyl content in calculating, from the alkali consumption, the percentage of dicarboxylated end-group in laminarinic acid. Some laminarinic acid obtained by oxidation of laminarin with bromine, then with periodic acid and finally with bromine again, contained no greater amount of carboxyl than when the first oxidation with bromine was omitted.

It is clear, therefore, that under the conditions applying during these oxidations, a certain modification of a limited number of terminal aldehydic hexose units does take place. The extent of this modification, however, is fixed and if allowance is made for it, the proportion of terminal non-aldehydic units, after alteration by periodic acid and subsequent treatment with bromine, may be accurately measured.

The isolation of the oxidation products in these experiments is rendered particularly easy by the property of spontaneous precipitation possessed by laminarin. This property is not affected in any way by the modification taking place in the terminal units and the laminarin flakes out of solution during the oxidation in a form in which it is very sparingly soluble in cold water. No difference in the ordinary properties of the polysaccharide could be detected before and after the oxidations. The results obtained are shown below :

Neutralisation value*	2553	2474	2478	2642	2556	2554	2663	2424	2666; mean 2553
Mol. wt. from Ag salt†	2580	2421	2739	2730	2578	2637	2604	2613	— ; mean 2606

* Weight of laminarinic acid which neutralises 2000 c.c. of N-sodium hydroxide.
† Calculated from weight of silver laminarinate which contains 216 g. of silver.
Allowance is made in all cases for the carboxyl introduced into the aldehydic terminal groups by the bromine.

This chain-length of 16 units has not been confirmed so far by the Haworth–Hirst method of end-group assay. In only one of a number of experiments has fully methylated laminarin been found to give a detectable quantity of tetramethyl glucose on hydrolysis. In this case the proportion of end-group was calculated to be 1 in 73. It must be admitted, however, that 9 g. was the greatest weight of methylated material available in any of these experiments. When greater quantities of methylated polysaccharide have been accumulated, hydrolysis may be found to yield a greater proportion of tetramethyl glucose. This possibility is being investigated.

Whatever the results of these experiments, the obvious properties of laminarin appear to indicate a macromolecule of much less than 73 glucose units. As already described (Barry, *Sci. Proc. Roy. Dublin Soc.*, 1938, **21**, 56), laminarin deposited from aqueous solution is obtained in grains very sparingly soluble in cold water. On the other hand, it is precipitated from aqueous solution by alcohol as a white powder soluble in 65—70% alcohol and readily soluble in cold water. A concentrated aqueous solution may be obtained which is water-clear, non-viscid and easily filterable. It has since been shown that the addition of glycerol to the aqueous solution will postpone indefinitely the spontaneous precipitation of the polysaccharide. It appears, therefore, as has already been suggested (*loc. cit.*), that the aggregation of the laminarin in aqueous solution is a physical process and that the solubility of the polysaccharide is related directly to the size of the colloidal molecule. Evidence has been given in a previous paper which indicates a spiral chain of β-glucopyranose units for laminarin and the evidence here presented suggests that about 16 glucose units make up this chain. Such a molecule might be expected to have properties similar to those cited above. The evidence is, however, not sufficient to rule out the possibility of a looped-chain structure or some form of laminated formula for laminarin, such as has been postulated by Hirst and Young for rice starch (J., 1939, 1471). Estimates of the reducing power of the polysaccharide as measured by alkaline hypoiodite all showed that the terminal aldehydo-group does not react stoicheiometrically with iodine. This may be due to a modification of some of the terminal aldehydic units, such as the formation of a 1 : 6 non-reducing anhydro-ring, as has been suggested by Freudenberg in the case of other polysaccharides (*Angew. Chem.*, 1934, 675). With alkaline copper solutions the values obtained were conflicting and could not be reproduced.

This method of end-group assay would not be applicable as such to laminarin if a small proportion of the glucose units in the molecule were united by 1 : 4- or 1 : 6-glucosidic links, as each of these linkages would uncover a further point of attack to the periodic acid. In this event, however, the results would show that for each of these 1 : 4- or 1 : 6-linkages present, there is a chain of 15 units joined by 1 : 3-linkages. In the light of the view taken at present of the chain structure of polysaccharides, the presence of these other linkages does not seem very probable and it must also be taken into account that no trimethyl glucose other than 2 : 4 : 6-trimethyl glucopyranose has so far been detected among the hydrolysis products of fully methylated laminarin.

Experimental.

The laminarin was purified by six successive depositions from water (see Barry, *Sci. Proc. Roy. Dublin Soc.*, 1938, **21**, 615).

Oxidation of Laminarin with Bromine.—A solution of laminarin (2 g.) in hot water (100 c.c.) was cooled, bromine (3 c.c.) added, and the mixture shaken from time to time in a stoppered flask. After standing for 1 hour, the laminarin began to be deposited and the mixture was kept in the dark for 5 days. The excess of bromine was now removed by aeration, and the separated laminarin collected (centrifuge), washed with water, hot alcohol, and ether, and dried over sulphuric acid in a vacuum desiccator to a white ash-free powder (moisture, 6·3%). 1·0 G. (absolutely dry) of the product neutralised 11·85 c.c. of N/100-sodium hydroxide. In subsequent calculations of neutralisation values, this volume of N/100-alkali is always subtracted from the actual alkali required for neutralisation.

Oxidation of Laminarin (i) with Periodic Acid.—A solution of laminarin (13 g.) in hot water (90 c.c.) was cooled, 0·44M-periodic acid (100 c.c.) added, and the mixture kept in a stoppered flask. The laminarin began to settle in flakes almost immediately. 0·25 C.c. of this mixture immediately after making up required, after addition of excess of potassium iodide and acidification, 4·37 c.c. of N/10-sodium thiosulphate. This titre dropped after 8 days to 3·88 c.c. The liquid was now decanted, and the oxidised laminarin washed in the centrifuge with water until the washings were free from periodic acid. It was then washed with hot alcohol and ether and dried first over sulphuric acid in a vacuum desiccator and then to constant weight in a high vacuum at 90°. 1·0 G. required 15·00 c.c. of N/100-sodium hydroxide, indicating that a small fraction of the aldehydo-groups had been oxidised to carboxyl by the periodic acid itself.

Further Oxidation (ii) of this Product with Bromine.—The oxidised laminarin (10·7 g.) was dissolved in warm water (200 c.c.), bromine (5 c.c.) added to the cooled solution, and the mixture shaken intermittently for a few hours and then kept in the dark (7 days). The twice oxidised laminarin (laminarinic acid), recovered as described above, was indistinguishable in appearance from laminarin. 1·0 G. of the dry laminarinic acid neutralised, on boiling, 9·04 c.c. of N/10-sodium hydroxide (phenolphthalein) or after correction 7·86 c.c., *i.e.*, 2000 c.c. of N-sodium hydroxide would neutralise 2545 g.

Silver Laminarinate.—To the neutral solution from above, excess of silver nitrate solution was added, and the silver laminarinate precipitated by the addition of absolute alcohol (4 vols.) as a white flocculent material which turned brown readily on exposure to light. It was separated on the centrifuge, washed a few times with absolute alcohol and then with ether, and dried over sulphuric acid in a vacuum desiccator to a pale yellow powder (moisture content, 7·84%). 0·4624 G. (absolutely dry) gave on ignition 0·0380 g. of silver. A similar allowance (see above) being made for the carboxyl introduced into the terminal aldehydic unit by the bromine oxidation, this gives a molecular weight of 2578.

Oxidation with Periodic Acid of Laminarin which has been already oxidised with Bromine.—The material (1 g.) was dissolved in hot water (10 c.c.), and the cooled solution treated with 0·44M-periodic acid (10 c.c.). The titre (N/10-sodium thiosulphate) was reduced in 8 days from 4·00 c.c. to 3·82 c.c. The oxidised laminarin was recovered as before; 0·5 g. neutralised 17·00 c.c. of N/100-sodium hydroxide.

Conversion of this Product into Laminarinic Acid.—0·4 G. was dissolved in warm water (10 c.c.), bromine (0·4 c.c.) added, and the mixture well shaken. The laminarinic acid was recovered as already described. 0·2 G. (dry) neutralised

18·00 c.c. of N/100-sodium hydroxide. With the usual correction (see above) this gives for 2000 c.c. of N-sodium hydroxide a weight of 2560 g.

Glucose and Glyoxylic Acid in the Hydrolysate.—Laminarinic acid (0·5 g.) was heated with 5% hydrochloric acid (10 c.c.) on the boiling water-bath for 4 hours, the liquid neutralised with ammonia, and a little of it treated with phenylhydrazine acetate in the usual way. Glucosazone was formed in quantity. A further quantity of the neutral hydrolysate on treatment with casein and concentrated sulphuric acid gave a deep blue-purple ring between the two liquids. The colour spread in an hour through the solution.

Oxalic Acid in the Oxidised Hydrolysate.—About 1 g. of the laminarinic acid was hydrolysed as described above, and bromine (0·8 c.c.) added to the neutralised hydrolysate. After shaking, the mixture was kept for a week. The liquid was again treated with excess of ammonia and then with calcium chloride solution, yielding a small amount of precipitate, insoluble in dilute acetic acid, soluble in dilute hydrochloric acid.

Glyoxal in the Hydrolysate from Periodic Acid-oxidised Laminarin.—About 1 g. of the laminarin after oxidation with periodic acid was hydrolysed by boiling for ½ hour with 5% sulphuric acid (50 c.c.). The liquid was neutralised with barium carbonate; on addition of phenylhydrazine acetate to the filtrate a colourless crystalline precipitate separated in small quantity. This was recrystallised from aqueous alcohol, giving colourless jagged spear-shaped plates identical with glyoxalphenylosazone.

The author expresses his gratitude to Professor Dillon for his interest in this work and to the Industrial Research Council of Ireland, who financed the experiments.

UNIVERSITY COLLEGE, GALWAY. [*Received, May 18th*, 1942].

117. *The Action of Sodium Silicate on Manganous Salts in Solution.*

By ERNEST A. DANCASTER.

The action of sodium silicates on manganous salts in aqueous solution has been studied. This is not a simple double decomposition, *e.g.*, $MnSO_4 + Na_2SiO_3 = MnSiO_3 + Na_2SO_4$, but owing to hydrolysis of the sodium silicate the manganous salt reacts with the sodium hydroxide, so the precipitate consists of manganous hydroxide and silica.

WALCKER stated (*Quart. J. Sci.*, 1828, **25**, 371) that when a solution of sodium silicate is added to one of manganous sulphate a white precipitate is obtained. This was not closely examined, and it does not appear to have been further investigated.

An attempt has been made to prepare hydrated manganous ortho- and meta-silicates by this method. The manganous salts used were the chloride, $MnCl_2,4H_2O$, and sulphate, $MnSO_4,4H_2O$. The sodium ortho- and meta-silicates were prepared by fusing together the appropriate amounts of silica and sodium carbonate. A solution of $Na_2O,4SiO_2$ was also prepared by adding silica portionwise to a hot solution of sodium hydroxide to saturation, and filtering the solution. When this was evaporated to dryness, and the residue dried at 242° and fused, it contained SiO_2, 79·84%, and therefore corresponded closely to $Na_2O,4SiO_2$.

The precipitation was carried out with solutions of concentration varying from M to 0·02M, and at temperatures ranging from that of the room to the b. p.'s of the solutions. Some of the precipitations were carried out with the manganous salt in excess, and others with an excess of sodium silicate. In all cases a white, flocculent precipitate was obtained which gradually became pink, and finally dark brown when exposed to air. When the precipitation and filtration were carried out in a non-oxidising atmosphere a white gelatinous mass was obtained which rapidly became dark brown on exposure to air, yielding a mixture of manganese oxides and silica. When this mass was dried at room temperature in a non-oxidising atmosphere a whitish friable mass was obtained. This remained unchanged on exposure to air at room temperature, but rapidly darkened when heated, becoming black at 250°. No precipitation takes place in slightly acid solution.

As it was evident that the precipitate contained manganous hydroxide, the freshly precipitated mixture was treated with hot boric acid solution in order to dissolve out this hydroxide. The dried precipitate was also treated in the same manner. In both cases the white, insoluble portion was filtered off, washed, dried, and examined. It consisted entirely of silica, without any trace of manganese. As the precipitate had not been baked, a variable proportion of the silica also passed into solution.

As the precipitates contained varying amounts of water, determinations of MnO and SiO_2 gave very variable results. The ratio should be constant if the samples consisted of manganous silicate, but it varied from 0·509 to 2·668 when precipitation was carried out with sodium orthosilicate, from 0·428 to 1·109 when with sodium metasilicate, and from 0·098 to 0·302 when $Na_2O,4SiO_2$ was employed. The ratios should be 2·359, 1·0179, and 0·2948, respectively. The precipitate therefore appears to consist of manganous hydroxide and silica, and hydrated manganous silicates cannot be prepared by this method. Sodium silicate is hydrolysed in aqueous solution, and the manganous salts evidently react with the sodium hydroxide thus produced, the reaction continuing until the whole of the sodium silicate has been hydrolysed.

When the dried precipitate is heated to red heat in a reducing atmosphere, manganous silicate is obtained just as it would be if the appropriate amounts of manganous hydroxide and sodium silicate were mixed and so treated.

WIMBLEDON. [*Received, December 8th*, 1941.]

118. *The Decomposition of Zinc Chloride Double Salts of Diazonium Compounds by Alcohols and Phenol.*

By HERBERT H. HODGSON and CLIFFORD K. FOSTER.

Methyl and ethyl alcohols decompose the zinc chloride double salts of diazonium compounds normally, hydrogen or an alkoxy-group replacing the diazo-group according to the nature of the substituents in the aromatic nucleus. Phenol, however, gives rise to three simultaneous reactions whereby (*a*) chloro-compounds, (*b*) hydroxydiphenyls, and (*c*) diphenyl ethers are produced; reaction (*a*) predominates throughout and its

mechanism appears analogous to that given by Hodgson, Birtwell, and Walker, (J., 1941, 770) for the Sandmeyer reaction.

THE decomposition of the zinc chloride double salts of diazonium compounds by methyl and ethyl alcohols proceeds normally, replacement of the diazo-group by hydrogen or alkoxyl depending on the nature of the substituents in the aromatic nucleus; electrophilic (kationoid) substituents favour hydrogen replacement and nucleophilic (anionoid) groups favour alkoxyl replacement (cf. Saunders, "The Aromatic Diazo-Compounds," 1936, p. 144 et seq.). In the presence of zinc dust the influence of the substituents is overcome, and only the hydrogen reaction occurs. Hodgson and Marsden (J., 1940, 207), decomposing the stable compounds of diazonium salts and naphthalene-2 : 5-disulphonic acid by zinc dust, found that the hydrogen reaction proceeded in solvents which contain no hydrogen. Hence the hydrogen must have come from the sulphonic acid group. In the present case the hydrogen can only come from the alcohol, and the zinc appears to activate the alcohol in some way, thereby making the reaction violent in certain cases.

By the decomposition of diazonium salts by phenol Hirsch (*Ber.*, 1890, **23**, 3075) and Norris, Macintire, and Corse (*Amer. Chem. J.*, 1903, **29**, 120) obtained hydroxydiphenyl derivatives, and Hofmeister (*Annalen*, 1871, **159**, 191) observed the formation of diphenyl ether from benzenediazonium sulphate and dry phenol.

Zinc chloride double salts of diazonium chlorides have now been decomposed by molten phenol and in the cases where a nitro-group is not present in the aromatic nucleus of the diazonium chloride, three simultaneous reactions occur : (*a*) chiefly replacement of the diazo-group by chlorine, (*b*) formation of a hydroxydiphenyl, (*c*) formation of a diphenyl ether (Table II).

The three different mechanisms involved may be illustrated from the complex involving benzenediazonium chloride, $\left[\text{C}_6\text{H}_5\overset{\delta+}{\text{C}}\text{–}\overset{+}{\text{N}}_2\right]_2\overset{--}{\text{ZnCl}_4}$. The kationoid carbon $\delta+$ to which the diazo-group is attached reacts (*a*) with anionoid chlorine in the complex, whereby electron release to the carbon occurs with separation of neutral chlorine, evolution of nitrogen, and subsequent linkage of the aryl radical with neutral chlorine to form chlorobenzene, a mechanism analogous to that of the Sandmeyer reaction (Hodgson, Birtwell, and Walker, J., 1940, 770); (*b*) with the anionoid *p*-carbon atom of the phenol to form, by similar release of electron, etc., the 4-hydroxydiphenyl; (*c*) with the anionoid oxygen of the hydroxyl group of the phenol, whereby the diphenyl ether is produced.

The zinc chloride double salts of *o*-, *m*-, and *p*-nitrobenzenediazonium chlorides all coupled with the phenol to form *o*-, *m*-, and *p*-nitrobenzeneazophenol. This enhanced coupling power is due to the well-known stabilising effect of the nitro- on the diazo-group.

EXPERIMENTAL.

The double compounds of diazonium chlorides and zinc chloride were prepared by adding solid zinc chloride (20% excess of the theoretical amount) to the well-cooled solution of the diazonium chloride and washing the precipitate with a little ether before drying it in a desiccator. The best results were obtained when the volume of solution was kept to a minimum during diazotisation.

Decomposition of the Double Salts.—(a) *By methyl or ethyl alcohol.* The double compound (in amount equivalent to 15 g. of the diazonium chloride) was refluxed with alcohol (100 c.c.) until decomposition was complete as indicated by the absence of colour in a spot test with alkaline *β*-naphthol; *ca.* 75% of the alcohol was then distilled through a fractionating column, the residue steam-distilled, and the distillate extracted with ether or chloroform. The products from *α*- and *β*-naphthalenediazonium chlorides were twice fractionally distilled in steam, a good separation being effected.

(b) *By methyl or ethyl alcohol in presence of zinc dust.* The course of the reaction depended on the method of mixing the reactants; *e.g.*, when a mixture of the zinc chloride double compound of *o*-nitrobenzenediazonium chloride and zinc dust was treated with alcohol, a reaction of explosive violence occurred, fumes having the odour of nitrobenzene being evolved and a considerable amount of carbonaceous matter produced. When, however, the zinc dust was stirred or shaken with the alcohol (50 c.c.) and the double compound (equivalent to 10 g. of diazonium chloride) added slowly, rapid but not violent decomposition ensued, with evolution of much heat. Subsequent operations were carried out as in (a). The results of (a) and (b) for ten decompositions are Table I.

TABLE I.

Products of Decomposition of Zinc Chloride Double Salts of Diazonium Chlorides by Methyl or Ethyl Alcohol.

Diazotised amine in the double salt.	Product.	% (MeOH).	% (EtOH).	% (Zn dust and MeOH.	Zn dust and EtOH).
α-Naphthylamine	Naphthalene	43	45	66	68
	α-Naphthyl alkyl ether	36	34	None	
β-Naphthylamine	Naphthalene	41·5	49	63	61
	β-Naphthyl alkyl ether	35	31	None	
p-Toluidine	Toluene	Trace	Trace	59	65
	Tolyl alkyl ether	77	75	None	
o-Toluidine	Toluene	Trace	Trace	70	68
	o-Tolyl alkyl ether	70	73	None	
p-Chloroaniline	Chlorobenzene	Trace	67	64	60
	p-Chlorophenyl alkyl ether	65	Trace	None	
o-Chloroaniline	Chlorobenzene	71	69	67	66
o-Nitroaniline	Nitrobenzene	72	67	63	65
m-Nitroaniline	Nitrobenzene	64	65	60	63
p-Nitroaniline	Nitrobenzene	61	66	68	63
p-Anisidine	Anisole	No decomposition		70	67

(c) *By molten phenol.* The double salt (equivalent to 20 g. of diazonium chloride) was slowly added to molten phenol (40 g.) at 60°, the mixture being gradually heated after each addition until the evolution of gas ceased. Nitrogen and hydrogen chloride were evolved and the temperature was so regulated as to keep the reaction under control. In some cases, *e.g.*, β-naphthalenediazonium chloride, reaction occurred rapidly at 60°, in others only at *ca.* 130°. The mixture was then cooled to 60°, poured into an equal volume of water, and fractionally steam-distilled until all the phenol had been removed. Any solid fractions were washed with water to remove phenol; any liquid matter was extracted with a suitable solvent, and the extract shaken with aqueous sodium hydroxide and washed with water prior to removal of solvent. The non-volatile products usually included a substituted 4-hydroxydiphenyl and sometimes a diphenyl ether. The hydroxy-compound was isolated by either hot water or aqueous sodium hydroxide, followed by acidification at 0°, and converted into its acetyl derivative, which was hydrolysed with caustic soda solution. The filtrate was acidified, and the product crystallised from dilute alcohol and identified. The results for six decompositions are in Table II.

TABLE II.

Products of Decomposition by Molten Phenol of Zinc Chloride Double Salts of Diazonium Chlorides.

Diazotised amine in the double salt.	% Chloro-compound.	% Hydroxydiphenyl.	% Diphenyl ether.
p-Aminophenol	*ca.* 40	*ca.* 41	*ca.* 11
p-Anisidine	48	36	13
p-Chloroaniline	41	31	15
Aniline	40	26	20
α-Naphthylamine	46	29	20
β-Naphthylamine	44	35	18

When the zinc chloride double salts of *o*-, *m*-, and *p*-nitrobenzenediazonium chlorides were treated with phenol as above below 90°, there was no evolution of gas and only traces of steam-volatile matter were obtained. The residue, usually a mixture of tar and crystals, was first crystallised from alcohol and then from toluene, *o*-, *m*- and *p*-nitrobenzeneazophenols being obtained in almost quantitative yield.

In the reaction between phenol and the double salt of *p*-nitrobenzenediazonium chloride at 130—140°, nitrogen was evolved and the main product was a non-steam-volatile tar.

4-Chloro-4'-acetoxydiphenyl crystallised from aqueous alcohol in colourless plates, m. p. 72° (Found: Cl, 14·0. $C_{14}H_{11}O_2Cl$ requires Cl, 14·2%).

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, May 22nd* 1942.]

NOTES.

Preparation of 4 : 6-*Dimethoxytoluquinone.* By ALBERT E. OXFORD.

THE methylating action of diacetyl peroxide on quinones (Fieser and Oxford, *J. Amer. Chem. Soc.*, 1942, **64**, in the press; Oxford, this vol., p. 577) provides a shorter route to 4 : 6-dimethoxytoluquinone than those starting from *o*-toluidine (Aulin and Erdtman, *Svensk Kemisk. Tids.*, 1938, **50**, 42; Anslow, Ashley, and Raistrick, J., 1938, 439).

Pyrogallol was methylated and oxidised to yield an equal weight of 2 : 6-dimethoxybenzoquinone by Baker's method (J., 1941, 665). To a solution of diacetyl peroxide (3·6 g.) (Gambarjan, *Ber.*, 1909, **42**, 4010) in glacial acetic acid (320 ml.), 2 : 6-dimethoxybenzoquinone (6·0 g.; 18% excess) was added, and the whole stirred at 80° until the quinone had dissolved and then maintained at 100° until evolution of carbon dioxide ceased (40 mins.). The cooled brown liquid was poured into water (1250 ml.) and extracted twenty-one times with light petroleum (about 300 ml. each time) and twice with carbon tetrachloride. The first seven light petroleum extracts were evaporated to dryness, and the residue crystallised from a very little carbon tetrachloride (at 3°) and then from ligroin (b. p. 80—100°) to yield 0·5 g., m. p. 123—125° (lit., 125°). The last fourteen light petroleum extracts were concentrated to very small volume; the product that crystallised was recrystallised from ligroin to yield 0·6 g., m. p. 121—125°. The carbon tetrachloride extracts were concentrated, chilled, and filtered from unchanged 2 : 6-dimethoxybenzoquinone, and the remainder of the solvent removed. The residue was collected, after trituration with methanol, and crystallised from ligroin to yield 0·2 g., m. p. 124—125°. The total yield was thus 1·3 g. of almost pure 4 : 6-dimethoxytoluquinone, *i.e.*, about 20% of the theoretical. A final crystallisation from methanol yielded 0·8 g. of the pure quinone, m. p. 125—126°.

The carbon tetrachloride mother-liquor from the crystallisation of the product from the first light petroleum extracts was evaporated to dryness, and the residue, after trituration with methanol, was crystallised successively from ligroin, aqueous methanol, and ligroin to yield 0·05 g. of pure 2 : 6-dimethoxy-3 : 5-dimethylbenzoquinone, m. p. 134° (see Oxford, *loc. cit.*). An impracticably large excess of 2 : 6-dimethoxybenzoquinone would evidently be required in order to suppress dimethylation entirely.—LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, UNIVERSITY OF LONDON. [*Received, July* 31*st*, 1942.]

Preparation of 2 : 3 : 5 : 6-*Tetrabromobenzoquinone.* By HERBERT H. HODGSON and CLIFFORD K. FOSTER.

2 : 6-DIBROMO-4-NITROPHENOL (10 g.) in boiling 20% aqueous sodium hydroxide (50 c.c.) was treated with sodium hyposulphite (hydros) until the orange-red colour had almost vanished; on neutralisation, 2 : 6-dibromo-4-aminophenol separated as a white precipitate. This was immediately made into a paste with water (50 c.c.) and sulphuric acid (5 c.c., *d* 1·84) and treated at 5° with sodium nitrite (2·4 g. in the minimum quantity of water), 2 : 6-dibromo-4-diazobenzene-1-oxide (9 g.) separating (Found: Br, 57·8. Calc.: Br, 57·9%). The diazo-oxide (2 g.) was added slowly to bromine (2 c.c.) in glacial acetic acid (30 c.c.) at 80°, and the mixture heated at 100° until the excess of bromine had been removed. On cooling, yellow crystals (3 g.) of 2 : 3 : 5 : 6-tetrabromobenzoquinone separated, m. p., after recrystallisation from benzene, and mixed m. p. with an authentic specimen 300° (Found: Br, 75·5. Calc.: Br, 75·5%).

The authors thank Imperial Chemical Industries Ltd. (Dyestuffs Group) for gifts of chemicals.—TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, July* 11*th*, 1942.]

A Colour Test for Certain Carcinogenic Hydrocarbons. By E. B. Lisle.

Test papers prepared by steeping strips of pure filter-paper in a solution containing 4 g. of silver nitrate in 100 c.c. of water and 5 c.c. of a 0·08% solution of methylene-blue are dried and then soaked in a solution containing 2·8 g. of potassium bromide in 100 c.c. of water. The operations are carried out in a dark room, and the dried papers stored in a black glass airtight bottle. A drop of a solution containing 2 mg. of a hydrocarbon in 10 c.c. of pure toluene is placed on the almost white test paper, which is then illuminated with light, λ 4200—4400 A., for 5 minutes. In the presence of a carcinogenic hydrocarbon a blue-grey spot develops in many cases. 3 : 4-Benzpyrene, methylcholanthrene, cholanthrene, 5 : 6-*cyclo*penteno-1 : 2-benzanthracene, 1 : 2 : 5 : 6-dibenzfluorene, 9 : 10-dimethyl-1 : 2-benzanthracene, 1 : 2 : 5 : 6-dibenzanthracene afforded positive results. The non-carcinogenic compounds anthracene, chrysene, 1 : 2-benzanthracene, and faintly carcinogenic 9 : 10-dimethyl-1 : 2 : 5 : 6-dibenzanthracene gave negative results.—92, Durham Road, Blackhill, Co. Durham. [*Received, May 20th*, 1942.]

The Preparation of Certain 2-Thiolpyridine Derivatives. By Montague A. Phillips and Harry Shapiro.

The preparation of 2-thiolpyridine by the action of alcoholic potassium hydrosulphide on the corresponding chloro-derivative (Markwald, Klemm, and Trabert, *Ber.*, 1900, **33**, 1556) was considered inconvenient; the preparation of 5-nitro-2-thiolpyridine by this method, however, seems to be satisfactory (Rath, *Annalen*, 1931, **487**, 105; U.S. Pat., 1,753,658). Both these compounds have now been obtained by methods based on the work on alkyl *iso*thioureas by Johnson and Sprague (*J. Amer. Chem. Soc.*, 1936, **58**, 1348; 1937, **59**, 1837).

2-Thiolpyridine.—2-Bromopyridine (15·8 g.), thiourea (7·6 g.), and alcohol (50 c.c.) were refluxed for 1 hour; after cooling, aqueous ammonia (*d* 0·880; 30 c.c.) was added, the mixture kept for 5 days at room temperature, the alcohol removed under reduced pressure, and the residue acidified with acetic acid and extracted with chloroform. Removal of the solvent gave 2-thiolpyridine (7·5 g.), m. p. 116—120°, sufficiently pure for many purposes. Recrystallised from benzene it melted at 125° (yield, 5·3 g. or 47% of the theoretical).

5-Nitro-2-thiolpyridine.—2-Chloro-5-nitropyridine (Phillips, J., 1941, 12) (20 g.) was added to a solution of potassium hydrosulphide made by dissolving potassium hydroxide (15 g.) in methyl alcohol (300 c.c.) and saturating the solution with hydrogen sulphide. The mixture was refluxed for 1 hour, the alcohol removed under reduced pressure, and the residue dissolved in water (125 c.c.) and acidified (Congo-red) with hydrochloric acid. The precipitated thiol compound, dried in a vacuum, had m. p. 169°; Rath (*loc. cit.*) gives m. p. 171—172° (yield, 17·7 g. or 90%).

Both thiol compounds were identified and distinguished from the corresponding disulphides by the fact that they absorbed the theoretical amount of iodine to yield the latter, when dissolved in methanol.

2-(5-*Nitropyridyl*)iso*thiourea Hydrochloride.*—A solution of thiourea (7·6 g.) in alcohol (50 c.c.) containing 2-chloro-5-nitropyridine (15·8 g.) was refluxed for 1 hour and cooled. The crystalline solid obtained (18·0 g.; 77%) had m. p. 191° (decomp.), not raised by recrystallisation from alcohol (Found: N, 23·9; Cl, 15·0. $C_6H_6O_2N_4S,HCl$ * requires N, 23·8; Cl, 15·1%). Treatment of this water-soluble material, which is probably identical with the so-called "addition compound" of Surrey and Lindwall (*J. Amer. Chem. Soc.*, 1940, **62**, 1698) and from which they obtained 5 : 5′-dinitro-2 : 2′-dipyridyl disulphide, with excess of aqueous ammonia as described under 2-thiolpyridine gave a yield of 85% of 5-nitro-2-thiolpyridine.

2-(5-*Aminopyridyl*)iso*thiourea Dihydrochloride.*—The above nitro-compound (10 g.) was reduced by refluxing for 1 hour with stannous chloride (30 g.) and tin (18 g.) in concentrated hydrochloric acid (46 c.c.). After dilution with water (100 c.c.) and removal of tin as sulphide the filtrate was evaporated to dryness under reduced pressure. The residue, crystallised from alcohol, had m. p. 204° (decomp.) (yield, 5·0 g.) (Found: N, 21·5: Cl, 27·1. $C_6H_8N_4S,2HCl,H_2O$ requires N, 21·6; Cl, 27·4%). The amino-group is diazotisable.—Research Laboratories, Messrs. May and Baker Ltd., Dagenham. [*Received, May 22nd*, 1942.]

The Interaction of Dimethylaniline and Nitric Acid. By Herbert H. Hodgson and Gerald Turner.

The investigation was undertaken to confirm, correlate, and where necessary amplify existing information on the reactions of dimethylaniline with nitric acid. Seven concentrations of acid were used, *d* 1·52, 1·42, 1·34, 1·254, 1·12, 1·046 and 1·024, the reactions were all carried out at 0° (and some at other temperatures), and the amount of acid was always in excess of that required for trinitration of the dimethylaniline, *e.g.*, dimethylaniline (5 g.) with 100 c.c. of the acid except at *d* 1·024, where 200 c.c. were used.

The results illustrate the variation with concentration of the dual action of nitric acid, *viz.*, nitration and oxidation. The latter is substantial only around *d* 1·12; the former not only becomes predominant with increasing acid density, but is accompanied by expulsion of a methyl group, a process which becomes more facile as the density of the acid or its temperature increases.

With nitric acid of *d* 1·52 at −5° to 0°, the product was entirely *N* : 2 : 4 : 6-tetranitromethylaniline. Van Romburgh (*Rec. Trav. chim.*, 1883, **2**, 108) used the nitric acid in 98% sulphuric acid at temperatures up to 55°.

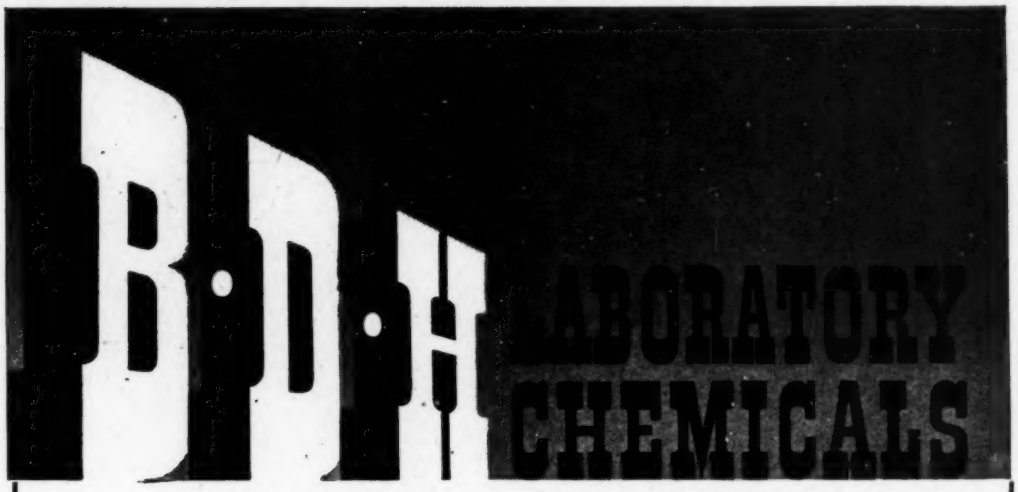
At *d* 1·42, only 2 : 4 : 6-trinitromethylaniline was obtained at 0°. At room temperature initially, a violent reaction occurred with rise of temperature and deposition of 2 : 4-dinitromethyl- and 2 : 4-dinitrodimethyl-aniline. Similarly, 2 : 4 : 6-trinitromethylaniline was obtained from 2 : 4-dinitrodimethylaniline.

At *d* 1·34 and at *d* 1·254, practically pure 2 : 4-dinitrodimethylaniline was obtained in almost quantitative yield at 0° in 30—60 minutes. When the temperature was allowed to rise, a mixture of 2 : 4-dinitromethyl- with some 2 : 4-dinitrodimethyl-aniline was formed. If the reaction mixtures with nitric acid of *d* 1·34 and 1·254 were kept overnight, all the product became 2 : 4-dinitromethylaniline.

The oxidising action of nitric acid was greatest at *d* 1·12, about 40% of the total yield being the alcohol-insoluble 3 : 3′ : 5′ : 5′-tetranitrotetramethylbenzidine. Mertens (*Ber.*, 1886, **19**, 2125; cf. also van Romburgh, *Rec. Trav. chim.*, 1886, **5**, 243) gives m. p. 240—260°. If the product is crystallised from nitrobenzene, however, orange-red prisms are obtained, m. p. 273° (decomp. 275°) (Found: N, 20·2. Calc.: N, 20·0%). The remaining 60%, soluble in alcohol, was mostly 2 : 4-dinitrodimethylaniline.

Nitric acid of *d* 1·046 and 1·024 did not react with dimethylaniline at room temperature during a fortnight, but on gradual addition of sodium nitrite *p*-nitrosodimethylaniline nitrate was precipitated (cf. Earl and Mackney, *J. Proc. Roy. Soc. N.S.W.*, 1933, **67**, 231) in amount almost equivalent to that of the sodium nitrite added, but always containing a small amount of *p*-nitrodimethylaniline (cf. Hodgson and Nicholson, J., 1941, 470). If excess of solid sodium nitrite was added fairly rapidly, small amounts of 3 : 3′-dinitrotetramethylbenzidine and *p*-nitromethylaniline accompanied the *p*-nitrosodimethylaniline.

* Surrey and Lindwall erroneously give the formula as $C_6H_7O_2N_2SCl$.



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